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A SIMPLIFIED INTERNAL TOCOGRAPH

BY

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IN the experiments to be detailed elsewhere in this *Journal* two different methods of tocography were employed. In a few cases, early in the puerperium, the external tocograph previously described (Embrey, 1955) was used. Mostly, however, the records were obtained in the second week of the puerperium by an internal method, using a recently developed modification of the original recorder. The instrument, as now modified, provides the facility of both internal and external recording of uterine motility.

METHOD

The principle of the internal method employed is to record graphically the pressure changes in a small intra-uterine balloon. This means of recording was first used as long ago as 1872 by Schatz, who introduced a large colpeurynter into the parturient uterus outside the membranes and measured the pressure with a mercury manometer. The method was later used to good purpose by Bourne and Burn (1927), who introduced a small rubber balloon (8 ml.) between the membranes and the uterine wall, and subsequently was modified by Moir (1932) for recording the contractions of the puerperal uterus. While not differing from these well-known and well-proven methods in principle, the tocograph to be described uses a simplified system of recording which, without any sacrifice of accuracy, obviates some of the inconveniences usually associated with internal tocography.

The intra-uterine balloon of 8 ml. capacity is connected by polyvinylchloride tubing to a suitable "Hydroflex" bellows which forms the recording head of the instrument and takes the place of the mercury manometer. This simple recording unit, comprising balloon, tubing and "Hydroflex" bellows, is depicted in Figure 1. It is fluid-filled and sealed and is calibrated in a pressure chamber against a mercury manometer. It can be easily sterilized by boiling and the unit is readily available at any time for immediate use. With the balloon introduced into the uterus the recording head slides into the appropriate channel of the tocograph and a single thumb-screw adjustment provides the required distension of the balloon (10–20 mm./Hg) before recording commences. The recorder is essentially the 3-channel instrument previously described in connexion with the original external tocograph (Embrey, 1955), but now provided with a variable speed drive and modified to accommodate either the internal or the external recording heads which are quickly interchangeable (Fig. 2). The tocograph thus becomes a combined internal/external recorder and provides, when required, the accuracy of internal tocography while still possessing to a surprising degree the great merit of convenience.

THE TOCOGRAPH IN USE

With the provision of a 3-channel recording unit, the study of records of intra-uterine pressure changes obtained synchronously from different parts of the uterus is facilitated. Whatever its merits in this connexion the internal tocograph has several uses as a single channel

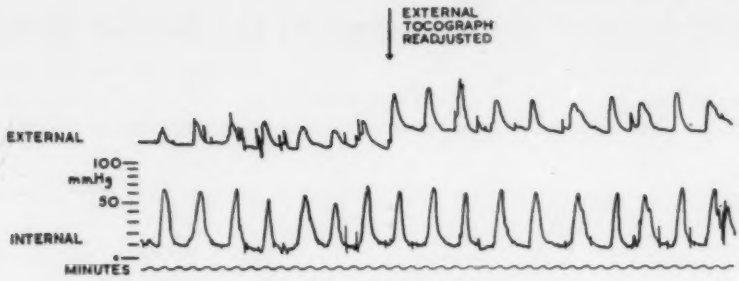

FIG. 3

A synchronous internal/external record. 1st stage of labour.

Note: External record influenced by slight movement and readjustment of receptor head.

recorder prior to or during labour. It can also be used to record uterine contractility in the puerperium and in this way provides an accurate objective method of determining the potency of oxytocic agents.

Records obtained with the internal tocograph show the expected graphic features of uterine contractility in different circumstances. They do not differ in any material respect from those obtained by the classical intra-uterine balloon-mercury manometer method of tocography, so do not require detailed description. A sample combined internal/external record is reproduced in Figure 3.

SUMMARY

A simplified internal tocograph is described. The instrument consists, in effect, of a modification of the previously described external tocograph so as to provide alternatively the facility of internal recording by the well-proven intra-uterine balloon principle.

The multichannel internal/external tocograph described in this paper is now known as the Oxford Tocograph. It is manufactured by H. G. East & Co., 37a Cowley Road, Oxford, to whom I am indebted for technical advice.

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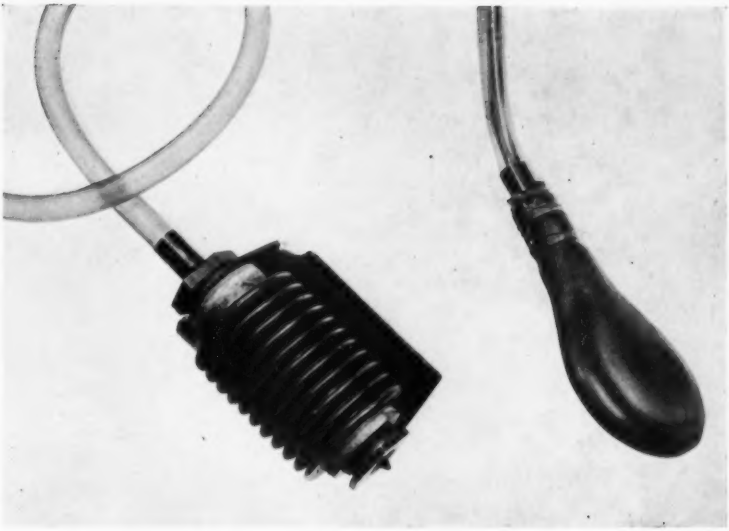

FIG. 1
The intra-uterine balloon and "Hydroflex" bellows comprising the recording unit.

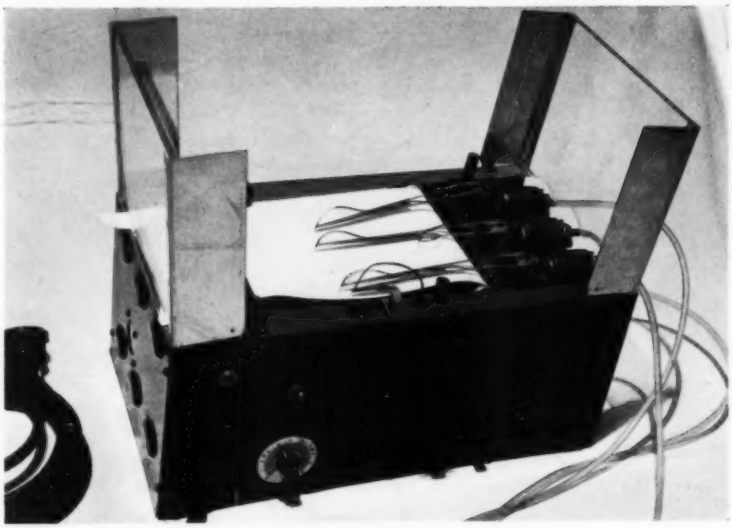

FIG. 2
The multichannel tocograph.

THE EFFECT OF ACETYLCHOLINE ON THE INTACT HUMAN UTERUS

BY

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IN 1937 Bell and Playfair carried out a clinical investigation of the value of acetylcholine in uterine inertia. Giving 0·2 g. intramuscularly 3-hourly for four doses they reported apparently successful results in 18 out of 23 patients. The stimulus of this report led to the drug achieving some popularity in the management of prolonged labour in the ensuing years, and, while it has never had pride of place in the obstetrician's armamentarium, authors of several standard textbooks still acknowledge its use in inert labour.

The premise on which the use of acetylcholine in labour is based was put forward by von Basch and Hoffmann (1877) and later supported by Whitehouse and Featherstone (1923), who maintained that the uterus (like the bladder and rectum) had a double nerve supply—the parasympathetic (*N. erigens*) supplying excitatory fibres to the longitudinal muscle and inhibitory to the circular coat, while the sympathetic (hypogastric) nerves inhibited the longitudinal and excited the circular muscle. The effects of parasympathetic stimulation are known to be brought about by liberation at nerve endings of acetylcholine which, on this view, might therefore be expected to augment the uterine contractions in labour.

However, the existence even of a parasympathetic supply to the uterus is in some doubt. For example, Langley and Anderson (1895), in dogs, failed to demonstrate any motor or inhibitory uterine effects on stimulating the sacral outflow of the autonomic nerve system. Physiological opinion is mostly that neither motor nor sensory parasympathetic connexions exist to the uterus, and while this view admittedly is based on animal experiments it cannot be ignored.

Founded as it is on a doubtful rationale the efficacy of acetylcholine as a stimulant of uterine contraction has not, in point of fact, been very well established. The clinical evidence is scant. Still more, tocographic confirmation of the value of the drug is singularly lacking. There are but few published records. A single tracing published by Moir (1935) failed to demonstrate any oxytocic effect of the drug. In another study (Embrey, 1940) experience in a few cases suggested that the drug (0·2 g.) was mostly without effect but might occasionally stimulate the uterine musculature by way of an increase in uterine tone. With a better appreciation of the limitations of external tocography, the evidence of increased tone would now be regarded as fallacious and the drug as without value.

It seemed appropriate therefore that acetylcholine should be carefully tested by tocographic experiment to determine its effect, if any, on the uterus. Especially did this seem desirable in view of the recent reports by Kaiser (1950) and Garrett (1954) clarifying the previously confused opinions in regard to the action of adrenaline on the human uterus. Garrett found that adrenaline (and noradrenaline) had to be given by continuous intravenous infusion to produce characteristic effects. Preliminary consideration of the matter suggested that acetylcholine would need to be administered in similar fashion. Even then it might be without effect. For unlike adrenaline, acetylcholine is not normally present in the bloodstream in any amount. Liberated at parasympathetic nerve endings, it is now known to be quickly destroyed by the enzyme cholinesterase so that the effect of even large doses intravenously might be expected to be evanescent.

In any event there was little indication of the appropriate dosage to be employed, though some guidance was obtained from the observations of Ellis and Weiss (1932) on the cardiovascular responses in man to intravenous acetylcholine. Having noted that small amounts produced effects in animals, these authors found that intravenously in man minimum effects were produced by 0·02–0·06 g. per minute, while they stated that the maximum tolerated dosage was 0·09–0·14 g. per minute. The effects were mainly subjective—flushing, palpitation, sweating. There was either no alteration or only a slight rise in cardiac frequency and some lowering of blood pressure in a minority.

Method

The suitability of the puerperal uterus as a test organ for assessing the strength of oxytocic agents has been demonstrated in several investigations and needs little emphasis. In this study acetylcholine was given by continuous intravenous infusion to 11 volunteer puerperal patients and the effect on uterine contractility recorded graphically. In two cases early in the puerperium the records were obtained by means of the external tocograph previously described (Embrey, 1955). In all other cases internal recording was employed using the Oxford tocograph described elsewhere in this *Journal*. During a control period an intravenous drip infusion of normal saline was set up. A second infusion apparatus was prepared but this time with the addition of acetylcholine in the saline solution (2 g. in 100 ml.). This was connected to the first set at the appropriate moment and adjusted to deliver the needed amount of the drug. Each experiment was closely controlled; subjective symptoms were noted while the pulse and blood pressure were recorded at frequent intervals.

Results

Sixteen doses of acetylcholine were given to 11 patients in the puerperium. The details of individual experiments are presented in Table I and typical responses shown in Figures 1 and 2. Initially the drug was used with great caution and in the first two patients the rate of infusion did not exceed 0·08 g. per minute, while the total dose was less than 0·2 g. In neither case was any effect on uterine contractions observed though subjective symptoms were evident.

Table I

Case No.	Dose: Grammes Per Minute	Dose: Duration (minutes)	Onset of Response (minutes)	Duration of Response (minutes)	
1	0·04	1·0	Nil	Nil	
2	0·08	2·5	Nil	Nil	
3	0·14	1·25	0·5	3·0	
4	0·16–0·22	5·5	0·5	5·0	
5 (a)	0·22	2·0	0·75	2·5	
(b)	0·30	2·0	0·75	1·5	
6	0·22–0·30	4·0	<0·25	5·5	
7	0·18	2·0	1·5	3·0	
8 (a)	0·20	1·25	<0·25	3·0	
(b)	0·22	3·0	<0·25	5·0	after atropine
9 (a)	0·28	3·0	0·75	3·5	
(b)	0·28	1·75	0·5	2·0	after atropine
10 (a)	0·28	1·0	<0·25	2·0	
(b)	0·30	1·75	0·25	2·5	after atropine
11 (a)	0·36	1·25	0·75	1·5	
(b)	0·36	1·5	1·0	1·5	after atropine

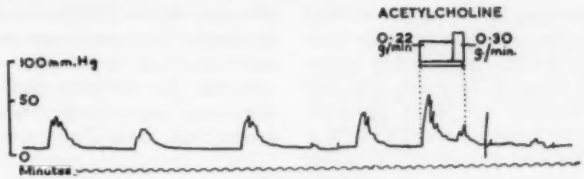

FIG. 1

Acetylcholine by intravenous infusion produces a uterine contraction. Note failure to maintain hypertonus even when rate of infusion is increased.

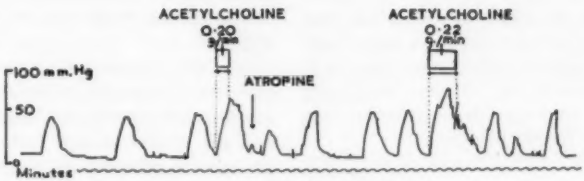

FIG. 2

Acetylcholine by intravenous infusion produces its characteristic effect. The uterine response to acetylcholine is unaffected by atropine.

In all other cases an oxytocic response was observed. With the acetylcholine infusion administered at rates varying between 0·14 g. per minute and 0·36 g. per minute a uterine contraction of considerable magnitude (usually increasing the intra-uterine pressure by 50 mm. Hg, or more) was produced almost immediately —to be precise within one minute. Depending on the length of the infusion the duration of the state of contraction varied between one and 5·5 minutes and in some cases appeared to be followed by a compensatory latent period. Because of the severity of the subjective symptoms administration of the drug could only be continued for a short period—the longest being 5·5 minutes.

As judged by a failure of the recording pen to return to the base line a state of hypertonus persisted as long as the infusion was running and, in varying degree, for periods of up to 2 minutes afterwards. However, attempts (in experiments Nos. 4 and 6) to maintain the uterine muscle in a state of complete spasm, comparable to the initial contraction, were only partly successful even when the rate of infusion was increased (Fig. 1). The maximum amount of acetylcholine administered in a single experiment was 1·1 g. in 5·5 minutes. In four cases (Nos. 8, 9, 10 and 11), after inducing the characteristic response to the drug, atropine was given in sufficient dosage to produce a pronounced atropinization effect and when this was evident the administration of acetylcholine was repeated. In each case an oxytocic response was again obtained proving that the acetylcholine effect is not blocked by atropine (Fig. 2).

The subjective symptoms were severe. Within a matter of seconds of the commencement of the infusion the patients were obviously flushed and complained of a sensation of throbbing in the head, and sometimes a feeling of constriction of the chest. There was an increase in lachrymation and salivation, while palpitation, sweating and nausea were other symptoms complained of in varying degrees. Fortunately these symptoms were short-lived and disappeared almost immediately on ceasing the infusion, while no untoward after-effects were noted. Mostly the subject noted a burning sensation at the site of venous puncture during, but only during, the injection.

Circulatory effects were observed in all cases.

Even with small doses (up to 0·14 g. per minute) there was a noticeable elevation in pulse rate. High dosage levels usually produced a correspondingly greater increase in pulse rate and also caused an elevation of blood pressure. With injection rates of the order of 0·2 to 0·36 g. per minute the pulse rate was mostly increased about 30 beats per minute, while, with the same dosage the blood pressure was invariably elevated—the systolic pressure approximately 20 mm./Hg, the diastolic pressure some 10 mm./Hg.

In the instances in which acetylcholine was administered after atropinization a significant difference in the general effects was observed. While the cardiovascular effects were still present obvious flushing, lachrymation and salivation were no longer evident.

Comment

The evidence presented in this investigation indicates that, providing it is given in sufficiently large dosage intravenously, acetylcholine can produce contraction of the uterine muscle in the human subject.

To produce this effect, however, it has to be given at the rate of more than 0·14 g. per minute which represents a phenomenally high and patently toxic dosage rate, and it would seem clear, therefore, that the drug can have no value in clinical obstetrical practice as an oxytocic. Moreover it is equally clear that, given subcutaneously in the dose which has usually been used (0·2 g. 3-hourly for 4 doses), it has no influence on uterine contractions.

The recorded experiments confirm the observations of Ellis and Weiss (1932) in so far as the effect of the drug is transient, while general symptoms are produced by doses of the order of 0·02–0·08 g. per minute. General effects are of course more marked as the dose increases and, in the range 0·14–0·36 g. per minute, include flushing of the face and upper trunk, throbbing in the head, sub-sternal constriction, palpitation, sweating, increased salivation and lachrymation, nausea and vomiting. Accompanying circulatory changes are usually evidenced by a marked rise in pulse rate and definite elevation of blood pressure, though Ellis and Weiss (1932) found only a slight rise in cardiac frequency and, in a minority, some lowering of blood pressure.

It may be observed that the dosage of the drug per kilogram body weight to produce these general and local effects is not only toxic but is far in excess of that required to produce similar effects in animals. Not only that, but it is of interest to note that it also exceeds greatly the dosage of adrenaline required to moderate its characteristic effect and has to be measured in grams rather than micrograms per minute.

The known effects of acetylcholine in the body include:

(1) "Muscarine-like" actions which are essentially the same as those of parasympathetic nerve stimulation and are abolished by atropine; and (2) "Nicotine-like" actions which include stimulation of sympathetic ganglia and skeletal muscle and the secretion of adrenaline by the suprarenals. These nicotine-like actions appear after the muscarine actions have been eliminated by atropine and in practice are not manifested except with large doses.

If this conception of the actions of acetylcholine is agreed then it may be reasoned from the experiments reported that uterine contraction following intravenous injection of the drug is not a parasympathomimetic action. This is suggested by the fact that the effect is only produced with very large amounts of acetylcholine while it is accompanied by some general effects (notably the cardiovascular effects—tachycardia and increased blood pressure) which are almost certainly nicotine-like. Again this view is supported by the fact that the oxytocic effect of the drug is not blocked by atropine. Of the general effects noted during the administration of acetylcholine, increased lachrymation, salivation and flushing are the most clearly "muscarine-like" and it is significant that in the experiments described these effects were blocked by atropine while the cardiovascular (and oxytocic) responses were not.

In the light of these observations there can be little doubt that the oxytocic response to a massive infusion of acetylcholine is not a parasympathomimetic phenomenon and is to be regarded as nicotine-like. Its exact nature awaits elucidation. It might conceivably be due to

liberation of adrenaline and noradrenaline by the suprarenals or by stimulation of sympathetic ganglia. Yet again the observation (Abrahams and Pickford, 1954) in animals, that administration of acetylcholine stimulates the neurohypophysis to release oxytocin (and vasopressin), invites speculation.

Whether this investigation has any bearing on the problem of the innervation of the human uterus is a matter for conjecture, for the evidence is indirect. Nevertheless, doubt as to the existence of a parasympathetic nerve supply to the uterus may be entertained, for it has to be put on record that the experiments here described failed to demonstrate any effect on the human uterus by acetylcholine which could be interpreted as parasympathomimetic. This observation lends itself, not unnaturally, to further speculation. Recent studies have helped to clarify the varying and seemingly contradictory reports of the effect of adrenaline on the human uterus and it has now been shown (Kaiser, 1950; Garrett, 1954) that in labour the uterine contractions are stimulated by noradrenaline and relaxed by adrenaline. Moreover, in animals at least, it has further been demonstrated that stimulation of the sympathetic nerves of the uterus results in secretion of both hormones (Mann and West, 1951). Now if uterine motility is influenced only by the sympathetic moiety of the autonomic nervous system the notion that normal co-ordinated uterine activity depends on a balance of the relative amounts of noradrenaline and adrenaline, as suggested by Garrett, becomes more plausible.

Summary

(1) By objective tocographic methods the effect of acetylcholine on the intact human uterus has been examined in 11 patients.

(2) In clinically permissible dosage even when given by continuous intravenous infusion, the drug has no influence on uterine motility.

(3) Only when infused intravenously in very high and manifestly toxic dosage is uterine contractility stimulated.

(4) The oxytocic effect is not blocked by atropine and is accompanied by general effects which indicate that it is a nicotine-like response and cannot be ascribed to parasympathomimetic action.

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SOME OBSERVATIONS ON THE INCIDENCE OF PRE-ECLAMPSIA

BY

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MANY believe that the mother's diet during pregnancy greatly influences the incidence of pre-eclampsia. In support of this point of view it is stated that the incidence of pre-eclampsia varies greatly from one part of the world to another coinciding with differences in dietary habits.

Before the accuracy of such statements could be checked international agreement would have to be reached concerning the definition of pre-eclampsia followed by epidemiological studies of clearly defined populations with differing food habits.

Unfortunately there are great practical difficulties in doing this since pre-eclampsia is difficult to define. It would be easier in some ways to study the incidence of eclampsia but this can usually be prevented by good antenatal care so that a varying incidence is more likely to be a measure of the efficiency of antenatal care than of the effect of more general environmental conditions.

Pre-eclampsia often causes no symptoms and many mild cases are not admitted to hospital. Careful blood pressure readings through pregnancy are therefore required in all cases. Ideally the patient's pre-pregnancy blood pressure should be known or at least the pressure in the first trimester, that is before pre-eclampsia has begun to affect it.

Quite a large proportion do not report to their family doctor or to a hospital antenatal clinic until well into the second trimester so that in these cases one cannot be sure that any hypertension found has arisen during the pregnancy. Another difficulty is that in a regional survey great variations in the technique of taking the blood pressure may invalidate to some extent conclusions drawn.

The present paper is a study of the incidence of pre-eclampsia in booked primigravidae in the Aberdeen Maternity Hospital during the years 1948–55. Since more than 90 per cent of all Aberdeen primigravidae are confined in hospital the group under review is fairly representative of all primigravidae in the City.

As a number of patients presented themselves at the clinic rather late it was not always possible to distinguish between mild pre-eclampsia and pre-existing hypertension. The definition of pre-eclampsia used by Nelson (1955) working in this clinic has therefore been used. He described pre-eclampsia as a condition in which a rise of diastolic blood pressure to 90 mm. of mercury or higher occurred after the 26th week of pregnancy on two occasions separated by at least one day or showed a progressive pattern if the rise occurred in labour. The interval between the readings should not, however, be so long that a definite relationship cannot be inferred. In the mild form, there is no albuminuria, unless of a trivial or transitory kind. In "severe" pre-eclampsia, in addition to the raised blood pressure there is albuminuria exceeding 0·25 g./litre (Esbach), preferably in a catheter specimen of urine.

Although oedema is commonly part of the pre-eclamptic syndrome, it is ignored for the purposes of definition and classification, since there is no satisfactory method of assessing degrees of oedema, and some swelling of the lower limbs is frequently found without any other evidence of pre-eclampsia. Furthermore, objective measurements of oedema are not usually undertaken in routine antenatal clinics and records of the clinical impressions of different observers are seldom consistent or reliable. Nelson's definition of pre-eclampsia

has since been used in Aberdeen in studies of weight gain and diet in primigravidae (Thomson and Billewicz, 1955, 1957), and a modification of it, distinguishing degrees of albuminuria, was found useful in an investigation of birth weights in pre-eclampsia and in normal pregnancy (Baird, Thomson and Billewicz, 1957).

This further experience has confirmed the usefulness of this criterion, although, as already noted, "mild" pre-eclampsia, thus defined, is often difficult to distinguish from other mild hypertensive states owing to the absence of blood pressure readings early in pregnancy in some cases.

Again the blood pressures were taken by a number of observers and it was not possible to standardize their techniques under the conditions of busy routine antenatal clinics.

Despite the simplicity of the definition used, and the fact that routine clinic records were used, the selection of cases of pre-eclampsia agreed closely with selection on more general clinical grounds. The only exception was that many "mild" cases of pre-eclampsia—those with a blood pressure raised to 90 mm. Hg or slightly over shortly before or during labour and with no other evidence of abnormality—were seldom described as pre-eclampsia on clinical grounds in the case record.

The points investigated are the incidence of pre-eclampsia in (*a*) first and second pregnancies in the same patient, (*b*) in second pregnancies where the first pregnancy ended in abortion, and (*c*) in twin pregnancy.

Results

Table I shows that the incidence of severe and mild pre-eclampsia is 5·8 and 18·4 per cent respectively in primigravidae. As noted by Nelson (1955) the incidence of severe pre-eclampsia is little influenced by age except that it is slightly raised in women over 35 years of age. On the other hand the incidence of mild pre-eclampsia rises steadily but slowly until the age of 30 after which it rises rapidly. The incidence in a second pregnancy is much lower, 0·4 and 7·6 per cent respectively. Only 6 (3·7 per cent) of those who had severe pre-eclampsia in the first pregnancy had a recurrence in the severe form in the second pregnancy (Table II). Where mild or no pre-eclampsia occurred in the first pregnancy the chance of severe pre-eclampsia in the second was extremely slight, only 0·6 and 0·1 per cent respectively. The incidence of mild pre-eclampsia in the second pregnancy was unaffected by whether severe or mild pre-eclampsia had occurred in the first pregnancy, being 23 per cent in each. If the first pregnancy is normotensive the risk of mild pre-eclampsia is only 3·1 per cent in the second pregnancy.

It seems clear therefore that pre-eclampsia is essentially a disease of primigravidae and that an "immunity" to it is rapidly and effectively

Table I

Incidence of Pre-eclampsia in a Series of 2,872 Women in Their First and Second Pregnancies

Grade	First Pregnancy		Second Pregnancy	
		Per cent		Per cent
Severe	161	5·8	11	0·4
Mild	476	18·4	218	7·6
No pre-eclampsia	2,235	75·7	2,643	92·0
Total ..	2,872	100·0	2,872	100·0

Table II

The Effect of Pre-eclampsia in a First Pregnancy Upon the Incidence and Severity of Pre-eclampsia in a Second Pregnancy
(Percentages in brackets)

First Pregnancy		Outcome in Second Pregnancy		
		Severe	Mild	No Pre-eclampsia
Severe pre-eclampsia 161		6 (3·7)	37 (23)	118 (73·4)
Mild pre-eclampsia 476		3 (0·6)	113 (23·7)	360 (75·7)
No pre-eclampsia 2,235		2 (0·1)	68 (3·1)	2,165 (96·9)

acquired. Also the primigravida who does not develop pre-eclampsia in the first pregnancy seems to have a fairly effective "immunity" so that the risks of mild and severe pre-eclampsia in a second pregnancy are slight (3·1 and 0·1 per cent respectively).

By contrast, those primigravidae with pre-eclampsia have mild pre-eclampsia more often in a second pregnancy (23 per cent) and this is the same whether the pre-eclampsia in the first pregnancy is mild or severe.

"*Virtual primigravidae.*" Since it is evident from the above that a completed first pregnancy confers marked protection in a second pregnancy, it is of interest to see what happens when the first pregnancy ended in abortion. A search of the records for 1948–55 yielded 516 cases of a completed pregnancy preceded by one abortion. In these, 10 cases of severe pre-eclampsia (1·9 per cent) and 71 of mild pre-eclampsia (13·8 per cent) occurred. Thus the risk of severe pre-eclampsia is reduced by two-thirds and that of mild pre-eclampsia by one-third by a first pregnancy of short duration.

Twin pregnancy. Since the incidence of twin pregnancy is low, records of all booked primigravidae for the 18 years 1938–55 were studied; these yielded 160 cases of twin pregnancy and the incidence of severe and of mild pre-eclampsia was 29 and 25·3 per cent respectively.

Thus twin pregnancy increases the risk of severe pre-eclampsia by five times in a first pregnancy. Even more striking is the fact that when a first pregnancy (single) is normotensive the incidence of severe pre-eclampsia and mild pre-eclampsia in a second pregnancy (twin) is 13 and 26·2 per cent respectively in contrast to 0·1 and 3·1 per cent respectively when the second pregnancy is single.

Threatened abortion. In 166 primigravidae (single pregnancies), who had had a threatened abortion, the incidence of severe and of mild pre-eclampsia was 3·6 per cent and 13·3 per cent respectively.

Discussion

The results reported illustrate how considerably the incidence and severity of pre-eclampsia are affected by parity or multiple pregnancy.

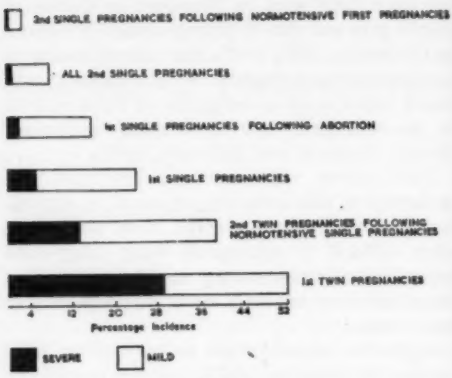

FIG. 1

Showing the incidence of pre-eclampsia with different types of pregnancy.

This is shown graphically in Figure 1. Taking the extremes, more than half of all twin first pregnancies developed pre-eclampsia, and about one-quarter severe pre-eclampsia, even though a high standard of antenatal care was provided and admission to hospital could be arranged at once when required; in fact, the great majority of cases of multiple pregnancy were admitted to hospital during the last trimester. By contrast, women having a second single pregnancy following a normal first pregnancy were almost immune; only about 3 per cent developed pre-eclampsia and it was severe in only 0·1 per cent of cases.

It seems clear that a first pregnancy confers considerable "immunity" since the incidence of pre-eclampsia is so low in a second pregnancy even in those cases where severe pre-eclampsia has occurred in a first pregnancy. The recurrence rate of severe pre-eclampsia is in fact less than 4 per cent. Even if the first pregnancy is of only short duration some immunity or adaptation develops although the protection is not so great as that following a full-time first pregnancy. It is not the occurrence of pre-eclampsia in a first pregnancy which protects the mother against the disease in her second pregnancy but rather pregnancy itself as witnessed by the reduced incidence in second pregnancies as a whole.

In fact, since about one-quarter of those who have pre-eclampsia in a first pregnancy have it again in the second it might be concluded that pre-eclampsia had not conferred protection in these cases.

However, one could postulate that those women who develop pre-eclampsia in their first pregnancy have a poor "natural immunity" to the condition and are thus more difficult to protect in the second pregnancy. The mechanism of this adaptation or immunity is obscure but that it begins to operate early in pregnancy is suggested by the fact that even an abortion in the first pregnancy decreases the risk of pre-eclampsia very considerably in a subsequent pregnancy.

The fact that threatened abortion does not increase the incidence of pre-eclampsia suggests that early placental damage may not be a factor in the production of pre-eclampsia even when it is sufficient to decrease the oxygen supply to the foetus in the later weeks of pregnancy (Turnbull and Walker, 1956).

This investigation confirmed the observations made by Nelson (1955) that social class and the height of the mother have little or no influence on the incidence of pre-eclampsia. From this it can be concluded that the variations in standards of health, physique and diet which still occur in Britain do not appear to influence the incidence of pre-eclampsia.

The apparent increasing incidence of pre-eclampsia, especially of the mild form, after 30 years of age in primigravidae may be due to the fact that in those women the blood pressure was raised before the onset of the pregnancy so that the diagnosis should have been essential hypertension instead of pre-eclampsia. As stated previously, some of the patients under review did not report early enough for this point to be checked. It is therefore being investigated.

The conclusion seems justifiable that there are considerable practical difficulties in determining the incidence of pre-eclampsia in any country or any area of it but they are not insuperable and the attempt should be made. Such studies would be of particular interest if the countries compared had very different methods of living and eating. Unfortunately in the under-developed countries adequate blood pressure readings are unlikely to be available and standards of medical care would probably differ greatly from those prevalent in Western Europe.

Summary

A retrospective study of case records of booked patients in the Aberdeen Maternity Hospital in the years 1948–55 has been used to study the influence of certain factors on the incidence of pre-eclampsia with the following conclusions:

(*a*) The condition is typically a disease of primigravidae, severe pre-eclampsia being about 15 times greater in a first than in a second pregnancy.

(*b*) When the first pregnancy ends in abortion the incidence of severe pre-eclampsia in the next pregnancy is only 2 per cent compared to 6 per cent in primigravidae.

(*c*) Twin pregnancy increases the incidence in primigravidae by 5 times and it is still high in a second pregnancy.

(*d*) Threatened abortion does not predispose to pre-eclampsia.

(*e*) Stature and social class do not influence the incidence.

(*f*) The incidence of mild pre-eclampsia seems to be increased in primigravidae over 30 years old.

Acknowledgments are gratefully made to Professor Baird and colleagues in the Midwifery Department and the Obstetric Medicine Research Unit (M.R.C.), Aberdeen, for their helpful advice and criticism.

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THE STRUCTURE AND ORIGIN OF THECO-GRANULOSAL TUMOURS

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THE present article gives an account of the study by multiple sections of 2 ovarian tumours—a typical theca cell tumour, and a variegated, mostly immature, theco-granulosal tumour. Its main purpose is to develop a principle whereby the origins of solid ovarian tumours may be definitively settled (as opposed to plausibly surmised) in adequately investigated, suitable material, and to apply it in the present context.

MATERIALS AND METHODS

The two tumours to be described were selected (as showing fairly clear results) from a larger number subjected to more or less extensive serial sectioning. Three paraffin blocks were made from the first tumour, and 18 from the second: about 1,250 serial sections were cut at 7 μ from the first tumour, and 3,300 from the vital (hilar) parts of the second. These were then dealt with by a uniform procedure: every twelfth section was automatically mounted and stained by Harris's haematoxylin and eosin; and the intervening sections were kept in their correct order and mounted and stained with this stain —or others indicated in the text or captions— where the findings warranted it. Some frozen blocks were also made. The material was fixed in 10 per cent formol saline.

FINDINGS

Case 1

Mrs. S.R., aged 73, complained of a pink vaginal discharge for 1 year and an episode of 2-days vaginal bleeding 1 week previously. She had been under treatment for 4 years for an extensive dermatitis, interpreted as seborrhoeic; and had been investigated also (in view of some frontal baldness and other suggestive features) as a possible case of myxoedema, with negative results. She had had the menopause 30 years earlier, prior to which she had menstruated normally and regularly, and had had 4 children and no abortions. Examination showed obesity, a few chest rhonchi, a bulky uterus, and a right ovary enlarged to the size of a hen's egg. Curettage showed a grade III adenocarcinoma and a benign mucous polypus of the cervix. A week later (9th July, 1953—Mr. Norman White) panhysterectomy was performed. Convalescence was complicated by some pyrexia due to infection, treated with sulphadimidine, streptomycin and penicillin: 4 years later she had no evidence of recurrence of the growth. The excised object consisted of a slightly enlarged complete uterus, with its cavity dilated by a soft whitish tumour springing mainly from the fundus and anterior wall, normal tubes, a right ovary with a protuberant hard walnut-sized fibrous tumour springing from its lateral pole, and an atrophic left ovary. Section of the uterine wall showed a cystic endometrial hyperplasia, passing by insensible degrees into a grade II–III adenocarcinoma, together with early adenomyosis.

Blocks were made roughly at right angles to the long axis of the right ovary, so as to extend through its whole thickness and that of the tumour; and these were cut serially throughout the whole region corresponding to the neck or pedicle of the tumour (its residual portions being used for frozen blocks). Figure 1 shows at low power a section through the middle of the whole object. At the bottom left is the pale attached portion of the broad ligament, and to the right of this is the main mass of ovary proper, with a pale medulla and a dark surrounding rim of hyperplastic ovarian cortex which extends both ways from the broad ligament to the neck of the tumour (or waist of the whole object—the split on the left is artefactual). The tumour (above) clearly has a nodular structure, with a central pale roughly triangular hyaline area. Just below this area is a knob of tumour projecting into the ovarian centre, the tumour as a whole being therefore pear-shaped; it has a just visible dark crescentic lower cap of ovarian cortical stroma. Elsewhere at the

tumour periphery remnants of ovarian cortex are seen as a dark rim at the upper left corner, and another and smaller one was seen at a deeper level at the top right. Being thus enclosed at five points by ovarian cortical remnants, and being also clearly separate from the medulla, the tumour may reasonably be inferred to have started as an intra-cortical mass which has grown and expanded eccentrically.

The nodules which formed the bulk of the tumour (its greyer parts in Fig. 1) consisted of closely packed, rather nondescript, roughly polygonal cells which gave a crowded impression (Fig. 2, below; Fig. 3, above and below). Individually they showed a weakly eosinophil, moderate cytoplasm and rather featureless nuclei: they lacked the ample granular cytoplasm and sharply defined, rounded vesicular nucleus of the typical lutein cell. The pattern of the argyrophil reticulum varied: that in the lower nodule of Figure 4 surrounds individual cells, and that in the upper one, whilst retaining a meandrine pattern, surrounds groups or trabeculae of cells. This is from a section adjacent and corresponding to that of Figure 3; which makes it clear that in an ordinary preparation the two patterns are not distinguishable. The spaces between the nodules consisted of poorly cellular connective tissue, which, in the extensive zone indicated in Figure 1, had hyalinized to a corpus albicans type of structure. At one point, corresponding to the stippled squarish area towards the right upper corner of Figure 1, the interstitial septa showed dark, interlacing connective tissue trabeculae, interwoven with pale cell-poor trabeculae (Fig. 2, upper), which form the other main thecoma pattern. This showed an exclusively pericellular reticulum; and both patterns showed in frozen sections throughout fine sudanophil intracellular droplets (Sudan IV), and more focally distributed doubly refractile lipoid.

The relation of the tumour tissue to that of the ovary varied. At the tumour hilus (the apex of the pear) the two tissues blended intimately. This region lies in the centre of the ovary in Figure 1, and is seen at somewhat higher power in Figure 6. This is from a section close to that of Figure 1, with recognizable corresponding landmarks, but the mirror-image reversal owing to being taken on a different machine: the crescentic or U-shaped lower cortical cap to the tumour is more clearly seen in this figure. Its junction with the tumour tissue above is shown at higher power in Figure 7, which is from the lowest point of Figure 6; the gradualness of the transition from the one tissue to the other is so evident that it is not entirely clear where one begins and the other ends. Figure 8 shows at higher power a reticulum impregnation of this region, showing, especially to the left, the same gradualness: ovarian cortex is seen below and tumour above. The occasional impregnation of tumour and not of ovarian cortical nuclei suggests empirically, according to general experience, the acquisition by the former of epithelioid status. In the tumour neck region (the waist of Fig. 1) the junction between the two was relatively abrupt, though the tumour was never "encapsulated" or separated by a distinct cell-poor collagenous layer. Figure 5 shows at higher power the right hand waist region of Figure 1. Below is seen tumour tissue, with ovarian cortical stroma above, presenting a fairly sharp edge over the right three-quarters. At and near the left-hand border this sharpness is less evident. The main difficulty lies in distinguishing ovarian cortical stroma from the darker condensed periphery of the tumour nodules (cf. Figs. 1–3). Distinguishing the two as well as possible, it was concluded that the junction between cortex and tumour was here always fairly abrupt, except where the plane of junction was very oblique to the plane of section. A few doubtful ovarian cortical rests were found within the main tumour mass, fusing intimately with it.

Figure 9 shows another part of the tumour hilus at a different level from that of Figure 7. Here the cap has attenuated almost to vanishing point, so that tumour tissue or tumour-cortex mixture above abuts fairly directly on the pale medulla below and to the left; more convincing cortical remnants were present on either side of this figure. Along the oblique left-hand border of the tumour are seen two triangular nests of small lutein cells of theca-lutein type; and below to the right is a bundle of smooth muscle cells (identified in phosphotungstic acid haematoxylin preparations by the presence of longitudinal myofibrils similar to those of Fig. 19). Similar lutein cells, singly or in small clusters, often strung out into line, were found in all that part of the ovarian cortex which bordered the tumour tissue (as occasionally were smooth muscle cells), sometimes in the internodular septa of the tumour, at all points throughout the hyperplastic right and similar left ovarian cortex, and most prominently at the tumour hilus, where they often contained a little brown pigment. There were prominent nests of hilus cells in both mesovaria.

Case 2

Mrs. E.D., aged 43, complained of very frequent periods (3–4/14) for about the last 6 months, which had supervened on 7 months amenorrhoea. Her periods had previously been regular (3–4/28): she had had no children and no abortions, having been married 3 years. On examination, the only noteworthy finding was a lower abdominal mass rising out of the pelvis. Panhysterectomy was performed (13th June, 1951—Mr. Norman White) at the Royal Northern Hospital. The excised object consisted of a small uterus, with one small fibroid and a large cervical erosion; a left ovary containing follicle cysts; and a right ovarian tumour. Only the last was available to me for investigation: it consisted of a multilocular tumour about 13 cm. in diameter, with a matt white outer surface suggesting ovarian tissue, and a cut pedicle visible on its surface. The outer wall varied from 0·5 to 5 cm. in thickness: both it and the interlocular septa were of white fibrous appearance on section, mostly enclosing like a sandwich a central yellow streak. In places (mainly hilarwards) this expanded to form large, rather soft, butter-yellow masses. At the actual hilus, below the cut edge of the broad ligament, tumour tissue fused intimately with a substantial knob of obvious ovarian remnant. Eighteen paraffin blocks were made from all parts of the tumour: 5 of these were cut serially,

3 of them from the hilus. All included, at some point, part of the outer wall.

The general architecture of the tumour is indicated in Figures 13 and 14. In 17 of the 18 blocks made the outer part of the wall consisted (apart from the cut edge of the broad ligaments) of more or less stretched ovarian cortex, identified presumptively in 9 on general appearance, and in 8 more definitely from the presence of primordial follicles. At all points (except the one indicated in the middle of Fig. 14 and later to be discussed) this was separated from the outermost layer of tumour tissue by a paler zone of poorly cellular connective tissue: the tumour was, therefore, central or medullary in situation. Its histological pattern varied: the commonest type was reticulate (Fig. 17). This might in appearance be epithelial or mesenchymal, stylized or untidy, massive or narrow and spun out: Figure 17 gives some idea of the variation. Figure 18 shows at higher power a silver impregnation of its upper, more massive part; and reveals a dense pericellular reticulum and rather numerous capillaries. Such patterns made up most of the tumour, especially round the periphery and in the narrower septa. Intracellular fat droplets (Sudan IV), mostly small, were found virtually throughout this pattern, varying in concentration from place to place, and scantier, more focal, doubly refractile lipoid was also seen. In the more solid areas lying towards the hilus, and seen in the more central parts of Figures 13 and 14, other patterns appeared: Figure 12 shows a silver impregnation from the centre of this region, with much variation of reticular pattern. Below is the edge of a mass of uniform cells (interpreted as granulosal), with little reticulum amongst them and condensed reticulum at their upper margin: above, this is continuous with a variable meshwork surrounding sometimes individual cells, sometimes a few, sometimes distinct nests. It can be seen that the more substantial collections tended to show nuclear impregnation with silver, which (as noted) is usually an indication of the acquisition of epithelial or epithelioid status (cf. Fig. 8). In an ordinary H. and E. preparation this area appeared as a continuous dark sheet of cells, the presumed granulosal zones showing merely more artefactual splits (owing to lack of reticular reinforcement), and slightly larger and more rounded nuclei, than the rest. In a few places were found some more sharply defined and typical granulosal collections with microfolliculoid spaces (Fig. 11, lower and right). some large and some small, showing transitional stages to the coarsely reticulate pattern above (not unlike the upper part of Fig. 17). Narrow epithelial 2-celled cords were also present (Fig. 19, upper two-thirds), sometimes with transversely elongated antipodial nuclei and very occasionally the formation of a lumen. Aberrant patterns found were some patches of notably loose primitive mesenchymal tissue, especially in relation to such cords (Fig. 19, middle), somewhat resembling endometrial stroma; and a great deal of smooth muscle (Fig. 19, below; and Fig. 11, between the darker masses), showing characteristic longitudinal myofibrils with phosphotungstic haematoxylin. Such muscle was particularly common in the narrow peripheral dark rim of tumour (well seen in the upper part of Fig. 14); but it lay definitely within the tumour tissue proper, and was not (like the smooth muscle of Case 1) part of an adjacent ovarian stromal reaction.

Finally, both the general and intimate relations of tumour and ovarian tissue must be described: the former are indicated in Figures 13–16. Figures 13 and 14 are from different but adjacent hilar blocks: as these were cut in opposite directions, corresponding landmarks (where present) bear a mirror-image relation to each other—that is, they face one another as the figures are mounted. Figures 15 and 16 concern the central quadrangular patch of tumour in Figure 14 (seen at the upper end of a succession of small dark ovarian stromal patches): they are from the same block at two successively deeper levels and at higher magnification; but (being taken on another machine) are again reversed and so have the same orientation as Figure 13. The quadrangular patch can be seen in Figure 13 in the position corresponding to that in Figure 14; but it is smaller, artefactually split, and has a clear connexion with the seam of tumour tissue above it. Moving away from here (successively through Figs. 14, 15 and 16) this patch develops a roofing crescentic locule (just beginning in Fig. 14), and progressively separates itself from adjacent tumour and ovarian tissue. In Figure 16, from the edge of this block, it is virtually quite separate from either; so that it has in effect continued into this thick piece of wall as a separate limb of tumour tissue (here cut across) running more or less parallel to the tumour surface. It was not picked up in the next block (though other landmarks were), and presumably ended shortly after the point shown in Figure 16. The remains of the string of ovarian stromal patches seen in Figure 14 are seen at the bottoms of Figures 15 and 16: in the opposite direction they condense into the dark irregular stromal mass in the centre of Figure 13, which itself had a tenuous connexion with the outer-lying rim of cortex. This, therefore, comes down to meet the rising dark limb of tumour, as the latter comes up to meet it.

Actual blending of ovarian stromal and tumour tissue occurred at 3 distinct zones, corresponding to the lower, middle, and upper edges of the tumour limb referred to and figured: the findings are shown in Figures 20–24. Figure 21, from the lower edge, shows ovarian stroma above blending with nests of tumour tissue below so intimately that it is difficult to say where one begins and the other ends. Figure 22 is a reticulum impregnation of this region from an adjacent section: in the tumour (below) the nuclei have begun to impregnate, and the fibres separate to surround groups of cells rather than individual cells; but the transition is quite smooth, without reticular condensation or heaping up at the tumour border. In Figure 20, from the middle, tumour tissue is seen to the left, and separate ovarian stromal patches below and above to the right. Blending between the 2 tissues occurs in a narrow strand near the bottom left corner, almost in line with the plane of junction, and across it at the top in a more convincing way. At higher power the latter was similar in principle to Figure 21; and so was the reticular pattern to that of Figure 22.

FIG. 1

Case 1. Section through middle of whole object, showing pale mesovarium below to left; main ovarian remnant below to right, with pale central medulla and dark surrounding hyperplastic cortex; and nodular greyish tumour above, with central pale hyaline area, tumour projection below into ovarian centre, with small dark caps of residual cortex below this and at top left. H. & E. ×3.

FIG. 2

Case 1. Edge of speckled area near right upper corner of last at higher power, showing dark reticulate pattern above, and edge of grey nodule with crowded pale theca cells below. H. & E. ×90.

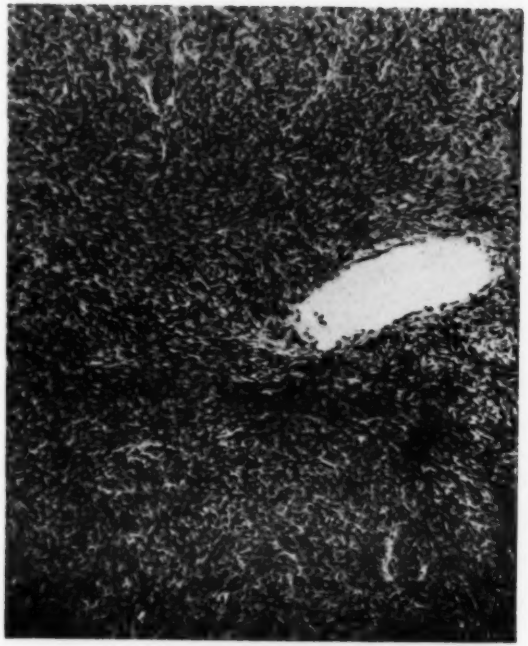

FIG. 3

Case 1. Edges of 2 nodules of similar appearance from middle of tumour, made up of crowded pale theca cells (above and below), with intervening septum containing venule. H. & E. ×95.

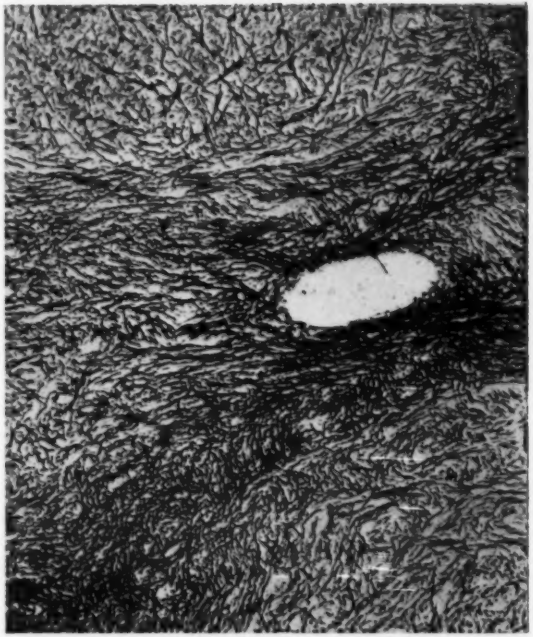

FIG. 4

Case 1. Section from same area as last, a few serials away, showing argyrophil reticulum of close pericellular pattern below, but surrounding nests and trabeculae of cells above. Modified Gomori. ×95.

FIG. 5

Case 1. From region corresponding to right-hand waist of Figure 1, showing, to right, hyperplastic cortex above presenting fairly sharp margin to uniform greyish tumour tissue below. At top left corner is a small dark narrow spur of cortex externally, the dappled tissue below and to the left of this being tumour with varying cell condensation. H. & E. ×22.

FIG. 6

Case 1. Proximal part of tumour from above ovarian centre in Figure 1, showing crescentic cortical cap below; and nodular tumour structure above with some intervening ovarian cortical tissue. H. & E. ×16.

FIG. 7

Case 1. Lowest part of last figure at higher power, showing ovarian cortical cap below blending intimately with tumour tissue above. H. & E. ×110.

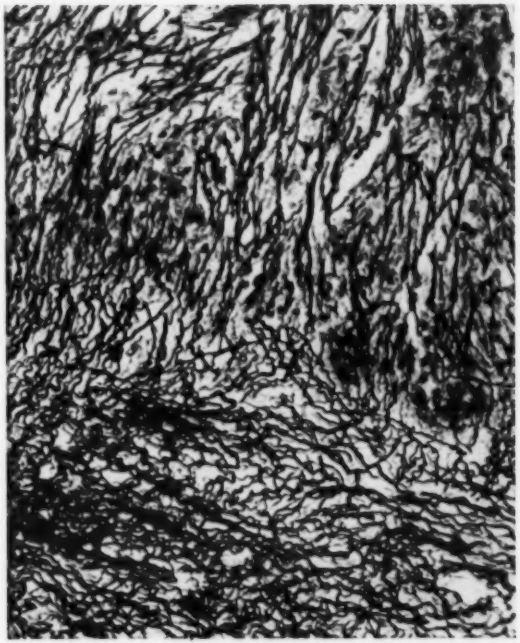

FIG. 8

Case 1. Reticulum impregnation of part of region last shown, from a nearby section, at higher magnification; showing ovarian tissue below and tumour tissue (marked by incipient nuclear impregnation) above, with absence of reticular condensation or heaping-up at their junction. Modified Gomori. ×180.

FIG. 9

Case 1. Same region as last 2 figures at a deeper level, showing tumour tissue above, medulla at bottom left, 2 nests of small lutein cells along oblique junction, and smooth muscle cells near bottom right corner. H. & E. ×175.

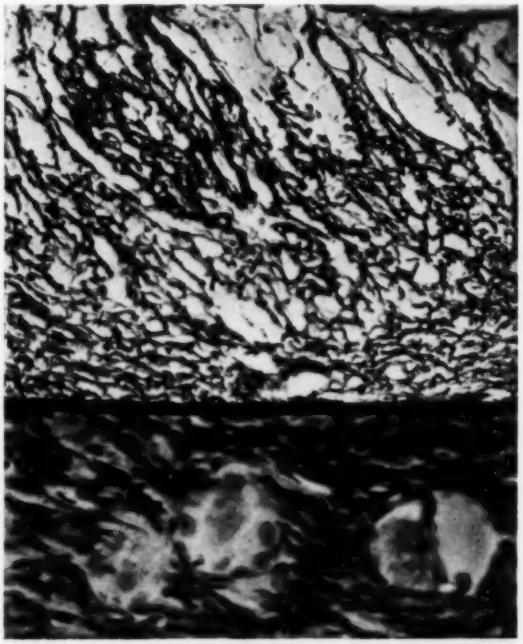

FIG. 10

Above—theca-lutein layer of atretic follicle from an ovary from a full-time pregnancy, showing reticulum with pericellular pattern below, but in places surrounding groups of cells above. Modified Gomori.

Below—3 primordial follicles; the 2 left cut tangentially, with stromal cells streaming across surface, the right showing apparent fusion of stroma and granulosa to left, and artefactual separation to right. For interpretation, see text. H. & E. Both ×300.

FIG. 11

Case 2. Coarse reticulate pattern above, passing, through ill-defined trabecular epithelial patterns (with intervening greyish smooth muscle bundles), into discrete granulosal masses (some of them with microfolliculoid spaces) below and to right. H. & E. ×55.

FIG. 12

Case 2. Showing edge of large mass of granulosal cells below, with condensed reticular border, blending with varied reticular pattern above, which partly encloses individual cells and partly variable small groups. From proximal part of tumour: note tendency to nuclear impregnation where tumour cells are grouped. Modified Gomori. ×175.

P.E.H.

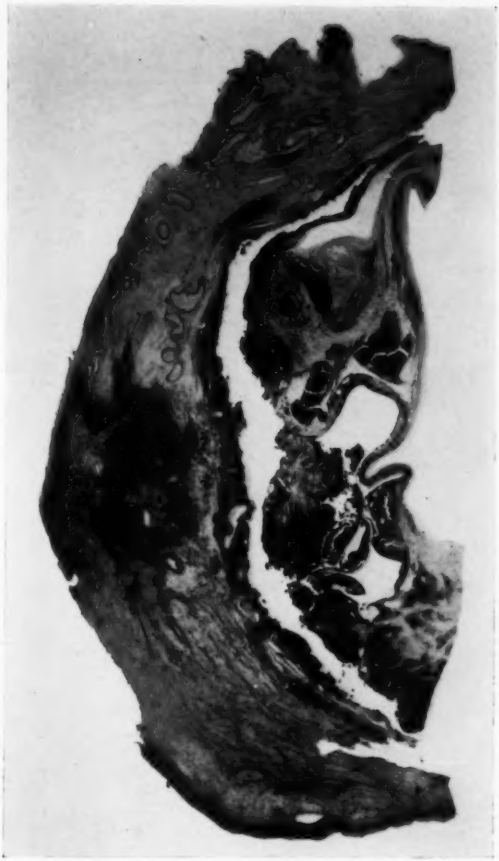

FIG. 13

Case 2. Hilar part of tumour at low-power, showing (on left) interrupted dark peripheral rim of cortex below and cut edge of broad ligament above; bordering this, on the right, the main ovarian mass (chiefly medulla, with irregular mass of dark hilar cortical stroma in the middle); and tumour tissue to the right again (the main mass of which has split off artefactually). H. & E. ×3.

FIG. 14

Case 2. The same region from adjacent block, with approximate mirror-image correspondence to last of certain landmarks. To right, dark ovarian cortical rim below, with cut edge of broad ligament above; medulla down middle of ovarian mass, containing a succession of small dark patches of hilar stroma ending above at a quadrangular patch of tumour which is beginning to separate off from the rest (above, below, and to the left of it). H. & E. ×3.

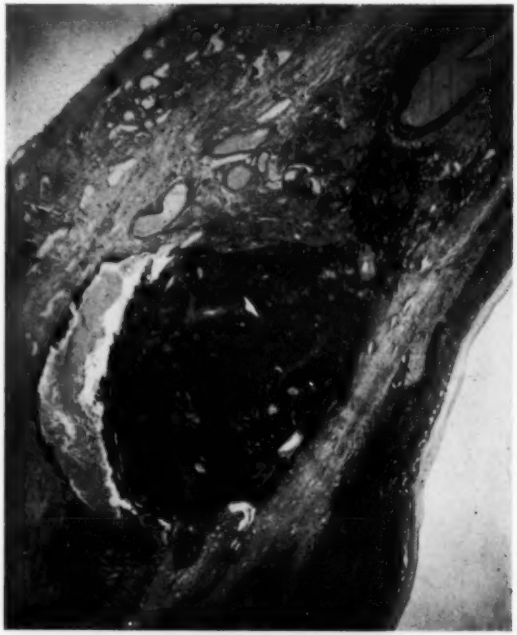

FIG. 15

Case 2. The region of the quadrangular patch from the last, at a deeper level (i.e., further from that of Fig. 13) at higher power (but with mirror-image reversal for technical reasons); showing beginning of segregation of dark central patch from adjacent tissues. H. & E. ×7.

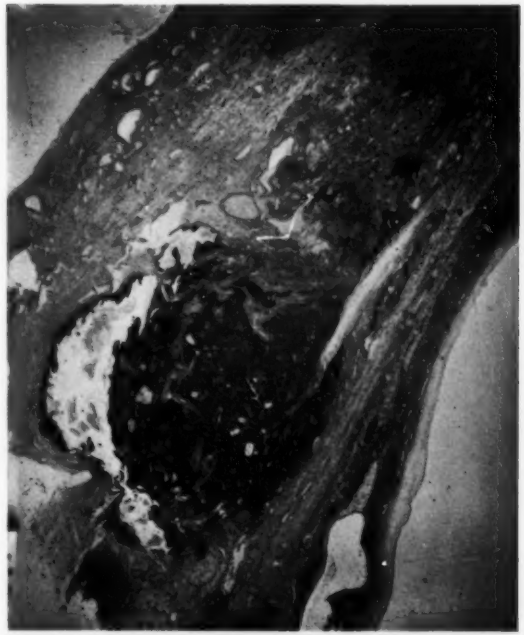

FIG. 16

Case 2. The same, at a still deeper level, showing well-marked segregation of dark patch from adjacent tissues. H. & E. ×7.

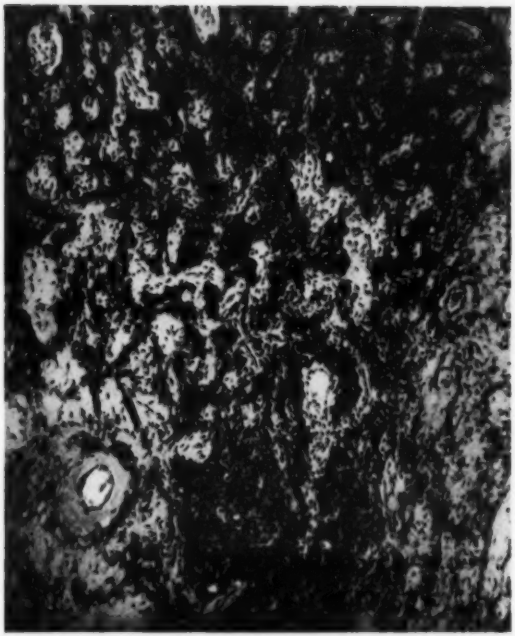

FIG. 17

A sample of the reticulate patterns which formed the bulk of the tumour, of massive epithelial appearance above, changing gradually into more delicate mesenchymal appearance at both lower corners. H. & E. ×85.

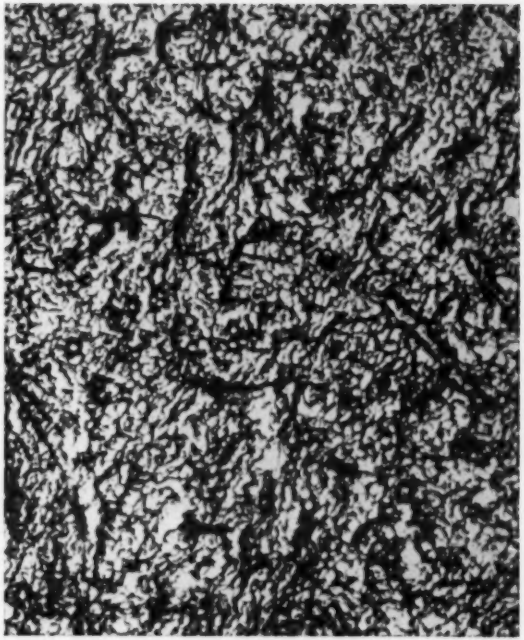

FIG. 18

Case 2. Reticulum impregnation of fairly massive part of last from a nearby section, showing numerous capillary reticular sheaths and intervening gauze-like pericellular reticulum. Modified Gomori. ×215.

FIG. 19

Case 2. An area close to that shown in Figure 11, showing smooth muscle with longitudinal striation below, and loose connective tissue in middle surrounding narrow two-celled trabeculae. Phosphotungstic haematoxylin. ×200.

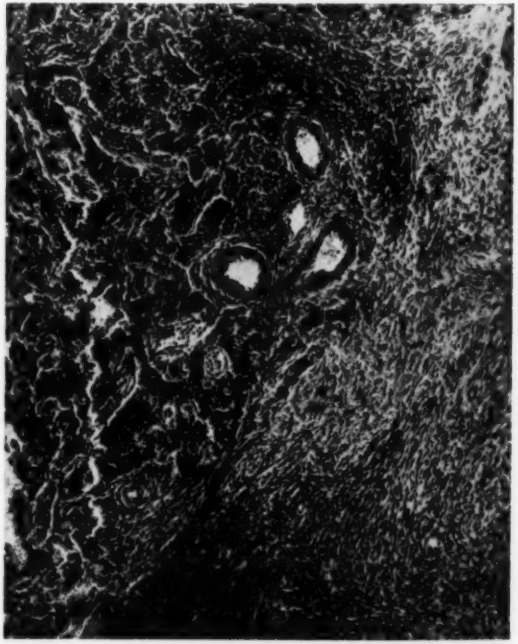

FIG. 20

Case 2. Region from proximal pole of tumour, showing nests of tumour cells to left, blending on right with 2 dark ovarian stromal patches above and below. H. & E. ×70.

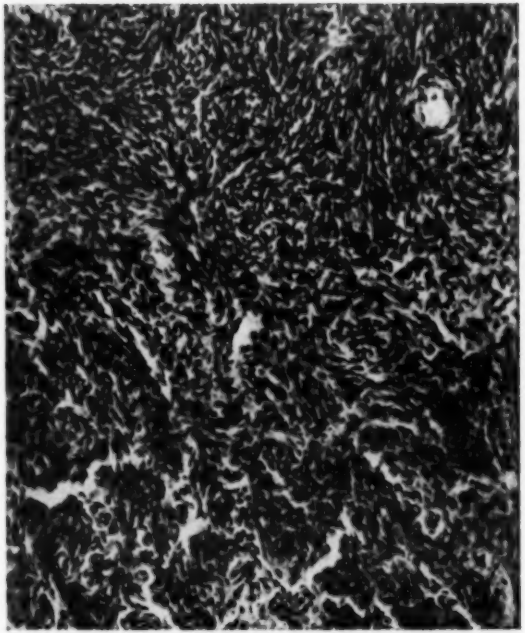

FIG. 21

Case 2. Another area from proximal pole, showing ovarian stroma above blending with nests of tumour cells below. H. & E. ×175.

FIG. 22

Case 2. Same region as last from a nearby section, showing pericellular ovarian stromal reticulum above, separating to enclose groups of tumour cells below, without condensation at the junction. Modified Gomori. ×165.

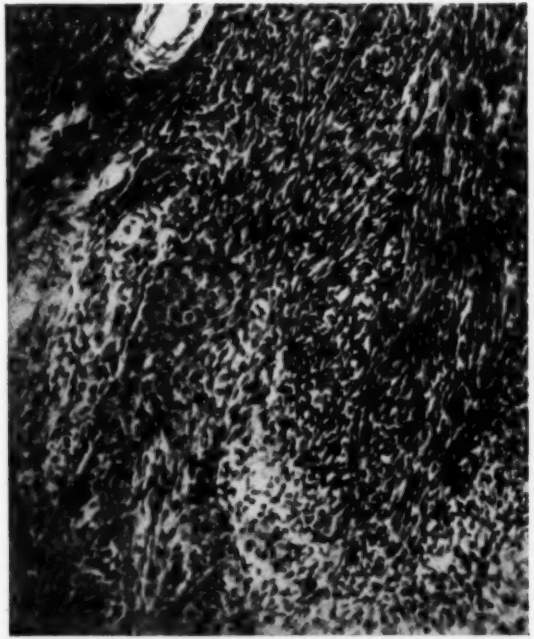

FIG. 23

Case 2. Another area from this region, showing ovarian stroma above and to right, blending obliquely across centre with arm of tumour tissue, which, beyond bottom left, gives place to pattern similar to that of Figure 21. H. & E. ×200.

FIG. 24

Case 2. Reticulum impregnation of same area from section close to last, showing pericellular ovarian stromal reticulum above, blending with that of tumour below, without junctional condensation. Modified Gomori. ×225.

In Figure 23, from the upper edge of the limb, ovarian stroma occupies the upper and right-hand half, and tumour tissue is present at the left lower corner (continuing off the figure into a pattern similar to that of the lower half of Fig. 21). An intimate blending between the 2 occurs over an oblique line running from the left lower to the top right corner. Figure 24 shows a reticulum impregnation of this region, tilted slightly anti-clockwise, but recognizable by its relation to the arteriole near the left upper corner: the character of the junction is similar in principle to that of Figure 22. Each of these 3 zones of transition was quite separate from the others, and the selected cross-sections shown are each taken from a continuous band of transitional appearances which varied in convincingness from point to point.

Two further findings from this transitional region need remarking on. Firstly, the patches of hyperplastic ovarian stroma concerned (such as are seen in the centres of Figs. 13 and 14) showed at several points, especially where bordering the tumour, little nests of lutein cells similar to those of Figure 9 from the last tumour; and, similarly also, they showed some patches of metaplastic smooth muscle formation. Both these were found only in this region and not (as in Case 1) throughout the cortex generally. Secondly, the tumour tissue concerned in the transition was of one type only, best seen in Figure 20 to the left and in Figure 21 below. This consisted of rather untidy granulosal nests and trabeculae of variegated polygonal cells with pale pink scanty protoplasm (giving a semi-luteinized impression): the whole pattern distinctly recalled that of a carotid body tumour. This tissue formed a discontinuous cap to the dark quadrangular patch shown in Figures 14–16, and blended with the tissue underlying it at several points. It must be emphasized that ovary to tumour transitions occurred only with this tissue and only in this region; which, in view of the large number of blocks made (mostly containing ovarian tissue) and the large number of sections cut, is particularly striking.

Discussion

There are four matters for discussion, namely, the structure, histogenesis, site, and pathological antecedents of these tumours.

Structure

The literature is now naturally very large, but the essential contributions which concern structure only can be enumerated briefly. The first unequivocal granulosal tumour was recorded by von Kahlden (1895); the name was conferred by von Werdt (1914); whilst the common vagaries of architecture were sorted out by Meyer (1918), who described folliculoid, cylindroid, and sarcomatoid forms, and this was later much expanded from his department by Habbe (1931), who described *inter alia* pseudo-adenoid, gyriform and reticulate patterns. Of uncommon but distinctive types, the first partially luteinized case associated with a uterine decidual reaction was described by Arnold, Koerner and Mathias (1930); Lecène's curious *folliculome lipidique* by Moulonguet (1932); and the first unequivocal partially adenomatous case by Amati (1932). An extensive account of the various patterns is to be found in the monographs of Schiller (1934) and Varangot (1937), whilst some eccentric examples have recently been published by Busby and Anderson (1954). The theca cell tumour was first identified as an entity by Loeffler and Priesel (1932) (though a number of earlier cases had been described), and the ensuing years established it as a hormone-secreting tumour. Its assimilation to the other went *pari passu* with the discrimination of the thecal and granulosal components of such tumours, and was largely the work of American investigators. The predominance of intracellular lipoid in the thecal elements was established by Greenblatt, Greenhill and Brown (1939) and McKay, Robinson and Hertig (1949); and the latter found a similar distribution of other relevant histochemically recognizable substances. The tendency of the argyrophil reticulum to enclose individual cells in thecal areas and groups of cells in granulosal areas was remarked by Traut, Kuder and Cadden (1939), Traut and Marchetti (1940), Henderson (1942), and Banner and Dockerty (1945). Both types of findings parallel those in normal Graafian follicles; and nearly all writers have stressed that the second distinction, though useful, is not absolute.

The last point is worth stressing. Figure 10 (upper) shows the highly luteinized theca of an atretic follicle from a full-time pregnancy: the reticulum surrounds individual cells below but at several points above surrounds groups—and this corresponds with the same variability in Case 1, Figure 4. In Figure 12 (from Case 2) both patterns are present, with all gradations between them, so intimately blended that it would clearly be impossible on this count to draw hard and fast distinctions between theca and granulosa cells. It is convenient also on other grounds to infer that many cells in these

tumours are of equivocal or mixed status: for example, marked stylization of pattern is, in general, a granulosal characteristic, but is often found in otherwise thecal areas. With this qualification, the patterns seen in these tumours can be interpreted as attempts to form, from a common stem, the 2 main components of the Graafian follicle, of varying maturity, in varying proportion, variously blended, variously abnormal in outline (owing to the simple fact of tumour formation), and with the variable development of structures probably to be interpreted as male homologues (see, for example, Mackinlay, 1957; cf., my Fig. 19). It is a pity therefore that the older term "folliculoma", because of its special association with a particular pattern, was displaced by the term "granulosa cell tumour", based on the dominant but misleading tradition of naming tumours after individual cells.

To this generalization there is a serious exception in the reticulate patterns (cf., Figs. 2 and 17) which are very common in these tumours: many are figured in Schiller's monograph. These are clearly not the product (as is a diffuse mesenchymal zone) of mere lack of maturity; nor do they seem to be aberrant imitations of any stage in the formation of a Graafian follicle or any homologue. Further, it was these patterns which were largely responsible for the application of such terms as "endothelioma" to many early cases; and they are paralleled closely in certain other tumours —notably salivary tumours and myo-vascular tumours allied to Stout's haemangiopericytoma. For example, Michaels and Langley's (1957) Figures 3 and 4 are clearly similar to my Figure 17. If Sheldon's (1943) belief in the importance of myo-epithelial cells in salivary tumours, and Stout's conception, are both accepted, then the common denominator of all 3 tumours is the development of a principal and an ensheathing cell from a common stem—that is, granulosa and theca, duct and myo-epithelium, endothelium and pericytes respectively. The pattern would seem therefore to be a neoplastic one *sui generis*, arising when this background is present; as if the structure (presumably a lattice-work in 3 dimensions) were determined to ensheathe something, if only loose connective tissue and a small vessel. The vascularity of this pattern (well seen in Fig. 18, in contrast to Figs. 22 and 24) is striking and clearly does not imply that the tumour is a vascular one. The development of smooth muscle in such tissue in a theco-granulosal tumour has not to my knowledge been described: it was remarked in the ovarian remnant attached to a thecoma by Nobili (1952, Case 2), in a manner somewhat like my Case 1. The analogous development of muscle in this way in Stout and Murray's (1942) original description of haemangiopericytoma was interpreted as an explicit morphological unmasking of the disguised muscular nature of pericytes: clearly the shift is much greater in the case of theca, for the human follicle does not normally have a muscular sheath.

Histogenesis

The origin of these tumours from the ovarian stroma—a view pushed by Schiller (1934) and accepted by Novak (1948)—is probably the theory most widely held at the present time. It may not be generally realized that it is largely a deduction from general principles rather than from observations made on the tumours: these principles derive from normal embryology and anatomy. Embryology (though often introduced) can be dismissed as irrelevant, for we are not here concerned with the potentialities of any constituent of the embryonic ovary: the relevant contention is that postnatal or adult ovarian stroma can give rise to theca (which probably no one doubts) and to granulosa (which is more debatable). There is little doubt that the source of the granulosa varies in different mammals (Mossman, 1938, 1952). Willis (1948) claims that in mammalian ovaries generally, including human ones, the intimate relation of the early flat granulosa to the surrounding stroma indicates that the first arises from the second; and Mossman (1952) takes the same view for rodent and human ovaries, regarding the ovum as inducing the change to granulosa. To my mind, the evidence of a transition from the one to the other is unconvincing; nor does there seem to be any reason why the neonatal ovary, each of whose primordial follicles already has its sphere of granulosa, should subsequently shuffle this with

the contiguous stroma and so produce such evidence. The lower part of my Figure 10 shows 3 primordial follicles in the ovarian cortex of a woman of 22. The follicle on the right shows (to its left) a suggestion of a transition between its flat granulosa and the surrounding stroma; but this diminishes on focussing up and down. Such a figure cannot clearly represent the difference between actual continuity and close overlying; and my impression is that if such follicles with apparent stromal-granulosal continuity are carefully examined the 2 elements are always found to be quite distinct. The 2 left-hand follicles of Figure 10 are cut tangentially and show this contrast well: it is only in an equatorial section that the 2 tissues look alike. The granulosal cells have pale rounded nuclei: cell outlines cannot be made out and may not exist, but (if present) would presumably be those of a polygonal plate. The contiguous elongated dark stromal cells appear as streamers across the surface of the follicle, as if forming a basket-work round it: the contrast of form is very evident. The arcuate separation of part of the granulosa from the surrounding stroma to the right of the right-hand follicle—due presumably to poor penetration of fixative in the dense cortex—is a well-known artefact. Its very commonness suggests that the granulosa is merely applied to the adjacent stroma, and is not attached to it (as the occurrence of interchanges between the 2 would imply). This is not to say that the adult stroma cannot give rise to granulosa, but merely that the evidence from normal tissue is unconvincing. It is far more to be expected that evidence of such conversion will be found in the tumours themselves, for tumour-formation is a great bringer-out of latent potencies. In any event it would be necessary to verify any theories on this point (if derived from elsewhere) in the tumours themselves; and to this notoriously difficult issue we must now turn.

The deduction of the histogenesis of an ovarian tumour can put little if any weight on analogies of structure alone between its pattern and that of some part of the ovary (as can be done with most other tumours). The fact that so many of them do not resemble any ovarian structure suggests at least the likelihood that all arise by heteroplasia of some unlike tissue. The starting-point must therefore be evidence of an intimate tissue blending, with cellular transitions, between tumour and ovarian tissue (as opposed to a more or less abrupt break, or even a capsule). Such blending in the case of individual theca cell tumours has been figured by Sternberg and Gaskill (1950) and by McKay, Hertig and Hickey (1953). The findings in the case of granulosal cell tumours are less clear; but Neumann (1925) described his second case as not sharply separate from its surrounding tissue, whilst Gospe (1936) stated that the sarcomatoid parts of his tumour "merged imperceptibly" with the ovarian stroma. Analogous findings from my 2 tumours are shown in detail in Figures 6–8 and 20–24. There is an intimate cellular blending of the 2 tissues, and the reticulum shows no heaping up, such as occurs often (though not always) when one tissue invades another. What follows? No one can deny that such findings are "suggestive" of an origin of the tumour tissue from ovarian stroma; but a firm inference is open to objections. Secondary tumours of the ovary (notably carcinomas from breast and stomach, and lymphosarcoma) often mingle their elements intimately with reacting ovarian stroma; and the variation of cell-type in each may produce a similar impression of the conversion of one into the other. It is well known that Krukenberg (1896) thought that the dusky and signet-ring cells of his tumour had arisen in this way: he wrote that "many pictures spoke in favour of a direct connexion of the cells with the elements of the stroma. Yet it must always be considered that such pictures can deceive . . ." (p. 314). In practice therefore such transitional pictures, by themselves, help less in regard to histogenesis than might be hoped; and the decision that a particular instance is a veridical or a "deceiving" one is really made in the light of general principles. And general principles in isolation are (like philosophy) little more than an unending battle of irreconcilables (of the type of "preformation versus epigenesis") in which the decision reflects the preference of the writer.

Awareness of this difficulty is almost as old as morbid histology, but it has been variously assessed: to some it appears as merely a minor inconvenience, to others an obstacle so serious

that it cannot even in principle be overcome. Bettinger (1953) cites the latter view in the statement "that one can never tell where a tumour came from, only what it looks like . . ." (p. 230); but the essential truth is that a statement as to where a tumour came from is a statement about its past. The problem is, in the very broadest sense, a historical one, concerned with the reconstruction of past happenings from the present traces they have left; and this is true even if the initial field of origin of the tumour is still contributing tissue to it up to the time of its removal. Moreover, the problem is an unavoidable one: if we had happened by chance to come across the tumour at about the moment of its inception, it would then be impossible to say with any confidence what it was going to become. We are dependent on getting a tumour old enough to be of quite definite nature, and not so old as to have obliterated all traces of its ancestry; and then reconstructing this ancestry from an adequate study of it. Naturally the results of such a reconstruction will not be known as directly or as certainly as the present appearances on which it is based; but they will not be known at all if the problem is misconceived. The existence and peculiar character of historical problems in biology has recently been discussed in general terms by Gould (1957). Unfortunately, pathologists (and others) often speak of transitional appearances of the type of my Figures 6–8 and 20–24 in terms which suggest that they are observing a process rather than a pattern: thus they will say that one tissue could be seen "changing into" or "giving rise to" the other. Such statements, taken literally, are false to the point of absurdity; and in practice, taken loosely, they serve merely to obscure the issue. (The much-used German word "Übergang", inasmuch as it conveys a more active impression than the English "transition", is particularly guilty in this way.) With the general character of the problem clear, it is now possible to consider (in the light of current methods of meeting similar ones) how it can be tackled.

Reconstruction of the past from present traces (whether done wittingly or not) is an integral part of the work of histologists, embryologists, and pathologists; and it is the essential part of that of historians, archaeologists, and palaeontologists, who are each concerned with something unique and unrepeatable. Since palaeontologists have made their subject into an integral part of biology, of unquestioned scientific standing, it is reasonable to ask whether there is anything relevant to be learnt from their procedure. The key, I think, lies in the fact that palaeontologists do not reconstruct an evolutionary tree by arranging the bones, etc., of extinct animals in a way that seems to them biologically plausible (which would be analogous to the way pathologists try to settle tumour histogenesis): they have an independent check on the supposed order of events in the existence of geological stratification. To put it slightly differently—with 2 independent criteria of the order of events to conjure with (though each is used to interpret each to some extent), they possess what seems in practice to be the touchstone of scientific status, namely, the (not too difficult) possibility of establishing correlations. (Thus Newell, 1956, wrote that "it is unimaginable that the physical and biological aspects of palaeontology could exist as separate disciplines. They are mutually interdependent.") Can something analogous be found for ovarian tumours? I believe the germ of an answer may be found in a remark of Robert Meyer (1930), made in another connexion, which may loosely but succinctly be translated as "No clear topogenesis, no clear histogenesis". (Ohne Klarstellung der Topogenese, keine solche der Histogenese.) The true parallel to stratification is to be found in the more or less radical revisions of architecture, in the expansions, separations, stretchings, and foldings (sometimes simple, often very complex) of the parent tissue which occur in tumour formation: these, if imaginatively reversed, give an indication of the source of the tumour. I would formulate therefore, as a key to ovarian tumour histogenesis, a "principle of histological and topographical congruence"; meaning at worst that the indications from the 2 sources shall be consistent, and at best that they shall point clearly and distinctly to the same site and the same tissue. This will now be elucidated by applying it to the 2 tumours described.

Figure 1, from the centre of the tumour of

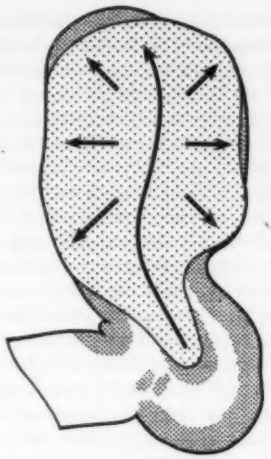

FIG. 25

Case 1. Diagram based on Figure 1, showing main growth movements which must have taken place in the tumour. The radiate arrows indicate expansile growth, and the central sinuate arrow movement away from the main ovarian mass. Reversing these, the tumour seems likely to have arisen near the lower end of the last arrow; and this is congruent with the site of histological blending between ovarian and tumour tissue. ×2.

Case 1, shows the simplest case; and Figure 25 is a diagrammatic version of this which (ignoring for the moment the secondary nodulation) indicates by arrows the types of growth that must have occurred. These are, firstly, simple expansile growth (represented by radiate arrows); and, secondly, a relative growth away from the main ovarian remnant (i.e., upwards as shown, and represented by the sinuate central arrow). Between them these suggest (by simply reversing the arrows and retracing the course of growth) that the tumour must have originated somewhere near the lower end of the central arrow; and this was where in fact the principal and most convincing histological evidence of blending and transition between tumour and ovarian tissue was found. The principle of congruence formulated establishes this region therefore as the site of origin of the tumour, and the cellular transitions shown as the mode of this. To elaborate: it is reasonably clear from the 5-cornered enclosure of the tumour by ovarian cortical remnants that it started as an intra-cortical nodule: so that, as it expanded and moved upwards, its tissue movement relative to the enclosing ovarian tissue would have tended to be greatest above and least below. Thus, transitions originally present at points other than the lower pole will tend to attenuate and get lost, the 2 tissues presenting therefore a more or less sharp border to each other, as in Figure 5. The fact of secondary nodulation introduces a complication: it implies the inclusion in, possibly (if rotation of the nodules occurs) the movement into, the interior of the tumour of non-neoplastic ovarian tissue; and these may as a result undergo little dislocation from the tumour nodules, with which they may consequently continue to blend. As the tumour was conspicuously nodular, this possibility was considered and looked for. The main difficulty was to distinguish included patches of ovarian stroma from the darker, more condensed seams of tumour proper, such as were commonly found between or encircling the main nodules (cf., Fig. 2): the difficulty is particularly apparent at the left upper corner of Figure 5, where both elements were judged to be present. It can be said, however, that areas found within the tumour which seemed most likely to be blendings between tumour tissue and included ovarian cortex lay wholly within its proximal part—that is, in the very nodular part shown in Figure 6. Finally, there has apparently also been (cf., Fig. 1) some centripetal movement of tissue here (slight in comparison with the main growth movement), which has somewhat stretched the underlying cortical cap, in places to vanishing point (cf., Fig. 9).

The second tumour is slightly more difficult to clarify; partly because by chance it was cut at right-angles to the optimal plane for showing the results in a single low-power photograph; and partly because later expansile growth has folded the tumour neck sideways. Successive cross-sections of this neck are shown in Figures 13–16; and a reconstruction of its course is shown in Figure 26, which is a diagram of the tumour topography comparable to that shown for Case 1. The reconstruction is impressionistic, and such details as the shape of

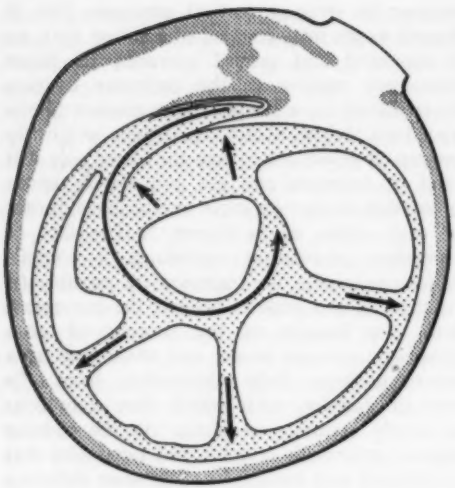

FIG. 26

Case 2. Diagram of second tumour based on Figures 13–16, to the planes of which its own is at right-angles: for details of relation, see text. Arrows (and inferences) as last; proximal pole of tumour is folded stem above; and projecting piece of top right border is cut edge of broad ligament. In both diagrams, closely stippled areas are ovarian cortex, sparser ones are tumour tissue, and plain areas are ovarian medulla or (within tumour) locules; in the second, the lower interlocular septa were relatively much thinner in the actual tumour. ×½ (approx.).

the locules are quite arbitrary: actual physical reconstruction (in wax or plasticine) is very laborious, and inevitably somewhat inaccurate at block junctions. All the sections mounted were carefully studied in the present case, and there is no reason to suppose that the inaccuracy in detail of an impressionistic diagram has any inferential consequence. The tumour in this case was medullary, and separated (in all blocks made) by a layer of cell-poor connective tissue and a layer of obvious or presumptive ovarian cortex from the exterior: its folded neck runs tangentially to the surface of the tumour before sinking in and connecting with the rest. The curved arrow starting in this neck indicates the main direction of growth of the tumour, whilst the radiate arrows indicate expansile growth as before: folding apart, the topography is roughly similar to that of the last. Thus, the direction of growth is inferred from the thick upper, and thin lower, ovarian capsule; coupled with the folding of the neck, which, unless the main lower tumour mass is a later formation, remains unexplained. Retracing the arrows, we arrive at the proximal part of the neck as the presumptive site of origin; and this is congruent with the site of the histological evidence of tumour and ovarian stromal blending shown in Figures 20–24. In this case there are no complications due to inclusion of ovarian tissue in the tumour: so that one must provisionally infer that the tumour arose from the hilar tongue of ovarian stroma seen in Figures 13 and 14. This tongue is invariably present in normal ovaries (cf., Fig. 1), but varies in prominence. In an earlier article a multiple sectioned arrhenoblastoma (which was reconstructed in plasticine) was traced to this tongue; and the principle of congruence here put forward was applied but not formulated (Hughesdon and Fraser, 1953): this tumour had in principle the same topography as the present one.

To defend and further elucidate the principle used, it is convenient to return to the simpler pattern of Figure 25 from Case 1. Blending of tumour and ovarian tissue occurred near the lower end of the central arrow; and this must have been either primary or secondary, reflecting (that is) either a local origin of the tumour or its subsequent invasion here. Now it seems clear that the main movement of the tumour relative to the ovary was upwards; so that if connexion had been secondarily established, it would have been least likely to have occurred in the oldest part below, and most likely above (where the latest, most vigorous, and most aggressive growth would be expected). Thus, one might expect in this case tumour-blending with the upper cortical caps of Figure 25. It must be admitted that one cannot do more than balance probabilities here. However, apart from these abstract considerations, there is the additional (and complementary) fact that secondary tumours of the ovary (which blend secondarily with ovarian tissue) do not actually do so preferentially at their site of origin in (i.e., entry into) the ovary, whether this be its surface or its vessels. To continue: it is clear that one

cannot establish congruences of the sort discussed without extensive investigation of the individual tumour—in practice, serial or step sectioning of all or vital parts of it. Even then, nothing will emerge unless the tumour has retained some sort of suggestive connexion with its host tissue. This will depend partly on simple mechanical growth (for adequate expansile growth is likely ultimately to snap all connexions), but also on other factors. Another small thecoma of mine (also largely reduced to serial sections) had an almost identical clinical background, morbid anatomy, and intimate topography with Case 1; but most of the tumour had hyalinized, the ovarian cortex was relatively inactive, and the evidence of histological blending with ovarian stroma near the tumour hilus was much less convincing. It would seem that the senescence of both tumour and ovary, and the consequent failure of what remained of the field of origin to continue adding to the tumour, obliterates the evidence of the tumour's ancestry as effectively as mere size. Hence it is a mistake to say (as is sometimes done) that what appears to be a histogenetically significant finding in one tumour is refuted by its absence in another similar tumour; for the reasonably exact comparability of the 2 (the essential condition of non-confirmation) need not be present. Finally, the principle of histological and topographical congruence has other possible forms than the one used—for example, between histological pattern and topographical site—and it runs into difficulties with the cystadenomatous tumours; but these points (having no present application) need not be pursued.

Site and Pathological Antecedents

It is difficult to discuss these apart from each other.

It is reasonably well established that thecomata are usually associated with the cortical hyperplasia and foci of stromal luteinization which become increasingly frequent with age, these conditions being usually present in the same and/or the opposite ovary (Woll, Hertig, Smith and Johnson, 1948; Sternberg and Gaskill, 1950; McKay, Hertig and Hickey, 1953). These were present throughout both ovarian cortices of my Case 1 (but only at the presumptive site of origin of the other thecoma just noted but not described). The natural inference is that thecomata are intra-cortical, probably arising in hyperplastic cortices in relation to lutein foci: Sternberg and Gaskill call them "the soil in which theca cell tumours are likely to develop". Direct evidence is scanty however: McKay, Hertig and Hickey figure a small thecoma merging with a hyperplastic ovarian cortex, and my Case 1 showed clear indications of its previous intra-cortical situation (as did the other thecoma referred to). It is clear, however, that when the tumour reaches any size it can hardly remain entirely within even a hyperplastic cortex, and must project either outwards (as did my 2 cases) or inwards into the medulla—an initial cortical origin being then a matter of reconstruction. Examples of this second development are figured by Loeffler and Priesel (1932, Case 1) and Nobili (1952, Case 2), and many authors refer more vaguely to encapsulation. If the anatomy of the tumour is as I have supposed, then it is not truly medullary in such cases: the medulla is in effect stretched round the tumour (as occurs in a typical cystadenoma).

With granulosal cell tumours there is more evidence but also more conflict. My Case 2 was medullary in situation, and apparently arose from a hyperplastic hilar (juxta-mesovarial) cortical tongue: from here it would be expected to grow most readily into the medulla, and less readily (but possibly) into the mesovarium. There is some literary precedent for this initial site and these 2 sequels. A number of small granulosal tumours are recorded; and in almost all in which the site is either stated or may reasonably be inferred, it has been central or medullary. Such tumours include those of Te Linde (1930, Case 3), Meyer (1931, VIII), Schulze (1933, Case 2), Kyank (1949), and Lau (1949, Case 1): also medullary was Meyer's (1931, VII), described as a "granulosal rest", but not apparently differing other than in name from a small tumour. Te Linde mentions a relation of his small tumour to the hilus, and small hilar tumours edging forwards into the mesovarium are described by Kermauner (1932) and Schiller (1934, Case 1). Some larger tumours have presumably taken this second course:

Willis (1948) figures a case in the broad ligament, and cites several others. Growth backwards into the medulla provides the tumours with a natural capsule; and accords with their commonly encapsulated state, and the relatively good prognosis which may well be partly its consequence. Estimates of the recurrence rate vary from about a quarter to a half of all cases (Busby and Anderson, 1954); which, though higher than once hoped, is clearly lower than ovarian carcinoma generally. Further, and also consistent with this, the literature gives the impression that local and lymphatic recurrence are relatively more important, and diffuse peritoneal dissemination relatively less important, than with ovarian carcinoma generally, though I know of no exact figures. It seems reasonable to suppose that the relevant antecedent pathology is a hyperplasia and focal luteinization of the hilar cortical tongue: this was present in my Case 2, and also in the arrhenoblastoma referred to as having a similar architecture; but I know of no other record.

There are, however, a few contrary indications. Giordano and Haymond (1944) recorded a small protuberant, presumptively cortical, granulosal tumour in a woman of 69, who had had hirsutism since puberty and also oligomenorrhoea until the menopause at 58. The status of this tumour seems to me open to question: being wholly luteinized and not of very distinctive pattern (in effect, a non-virilizing lipoid cell tumour), its earlier phases might have been thecal, granulosal, or neither. On the history, its background might earlier have been a pair of Stein-Leventhal ovaries, which (follicles apart) are somewhat analogous to Hertig's diffuse cortical hyperplasia of later life: the latter was present in the opposite ovary. An early granulosal tumour with contralateral diffuse (not merely hilar) pre-menopausal cortical hyperplasia was recorded by Schröder (1901) A medullary (and perhaps hilar) site might in the abstract be reached from anywhere in the cortex, if a developing tumour is made to sink inwards after the manner of a ripening follicle. There is some evidence for this if we take "granulosal rests" (or, in more contemporary idiom, "anovular follicles") to be an early or abortive stage of the same process as leads to tumour formation, for Meyer (1912) described the smaller examples of these as lying in the more central parts of the cortex and seldom in the medulla; whilst Blau's (1932) Case 7—a collection of such "rests"—was adjacent to the hilus, and appears to extend from the deeper cortex into the medulla. More recently, McKay, Hertig and Hickey (1953) have endeavoured to make atretic follicles with good granulosal preservation (and sometimes atypical granulosal proliferation) take over the pathogenetic role of Meyer's "granulosal rests". Such follicles may be found in any part of the cortex as well as deeper, and are not uncommon in Stein-Leventhal ovaries and in endometriosis. The idea remains only a suggestion, however, and one not easy to verify; for the presence in granulosal tumours of structures resembling atresing follicles (which the authors adduce in this connexion) surely carries no more inferential weight than imitations of other follicular forms. Their objection that an origin from ovarian stroma is too non-specific may perhaps be met by supposing that the medulla or the hilus exerts an inductive effect on proliferating tissue. In certain small mammals medullary follicles of peculiar structure are found in this region: thus Kingsbury (1914) describes them in kittens as being often odd in shape and showing cell columns with antipodial nuclei. I conclude that on the limited evidence available granulosal cell tumours are generally hilar in origin and medullary in site; and that, though it is possible that this topography is secondarily arrived at, the evidence is inconclusive.

Apart from site, the conclusion is that local or general ovarian stromal hyperplasia, with lutein foci (and sometimes other metaplastic changes), is the antecedent of both these tumours. The cause of this condition is unknown, though an excess of pituitary luteinizing hormone has been invoked. It possesses a distant analogy with the diffuse ovarian luteinization that occurs in irradiated rodent ovaries (Schiller, 1934; Geist, Gaines and Pollack, 1939), and in ovaries transplanted to the spleen (Biskind and Biskind, 1949)—that is, if one allows for the relatively higher stromal content of human ovaries. Both of these procedures may later result in theco-granulosal tumours. Irradiation

does not seem to be a causative factor in the human cases. Kyank (1949) recorded a granulosal tumour following irradiation, and collected 6 others from the literature, together with 2 thecomata; whilst McKay, Hertig and Hickey (1953) have recently described another such granulosal tumour, and cited a further one: but these must be a very small fraction of reported cases, and a very much smaller one of irradiated patients. The reason for the difference probably lies in the failure of the human ovary to respond to irradiation with the diffuse lutein changes seen in the rodent, according to Meyer (1921) and presumably general experience.

Summary

(1) A study by serial section of a thecoma and a theco-granulosal tumour (orientated towards structure, site and origin) is presented. The thecoma was essentially a projecting intracortical knob; showed condensed and reticulate cellular patterns; and blended proximally with remains of ovarian cortex, whilst presenting a sharp border to it elsewhere. The theco-granulosal tumour was medullary, with successive capsular layers of cell-poor connective tissue and ovarian cortex; showed a variety of patterns; and blended (at its folded proximal neck only) with a tongue of juxta-mesovarial cortical stroma.

(2) The literature of the structure of these tumours is reviewed, and the fallacy of relying unduly on the pattern of the reticulum fibres illustrated. All the patterns can be rationally interpreted as follicle-forming, with the exception of certain common reticulate patterns which recall those of some salivary and vascular tumours. These (often once called "endothelioma") are interpreted as a specific neoplastic pattern *sui generis*, resulting when a principal and an ensheathing cell are produced from a common stem.

(3) The histogenesis of an ovarian tumour cannot be deduced from its analogies of structure with ovarian or other tissues; and the fallacy of deducing it from an intimate blending of tumour and host tissue alone is discussed. Undue reliance on this has hidden the real nature of the problem, which is essentially one of reconstructing the past course of growth of the tumour from remaining indications: it is, in a broad sense, a historical problem, and the widespread occurrence of such problems in biology is noted.

(4) A "principle of histological and topographical congruence" is developed in the light of this; meaning that the topographical form and intimate histological relations shall at least be consistent in regard to, and preferably shall each point directly to, the same site and tissue of origin. In both the tumours discussed, the apparent direction of growth was away from the sites of tissue blending noted; which is congruent with these being the sites of origin. In the light of this, the thecoma arose from the stroma of the ovarian cortex; and the theco-granulosal tumour from that of the hilar (juxta-mesovarial) region: each bore a relation to a local or general stromal hyperplasia with lutein foci.

(5) The literature relating to the origin and site of these tumours is reviewed. It is generally agreed that thecomata arise from and within a hyperplastic ovarian cortex. Most small granulosal tumours have been medullary in site, and some have been hilar: this accords with their encapsulation and relatively good prognosis, and with the view that they arise from metaplasia of the hilar tongue of cortical stroma. It is also possible that they sink inwards from any part of the cortex, like ripening follicles; but the evidence as to this is inconclusive.

I am much indebted to Mr. Norman White for permission to publish these 2 cases, and for providing me with data about the second; to Sir Roy Cameron, F.R.S., for advice and encouragement; and to Mr. V. K. Asta for drawing Figures 25 and 26.

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ATTEMPTED TREATMENT OF A PATIENT WITH CHORIONCARCINOMA BY IMMUNIZATION WITH HER HUSBAND'S CELLS

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THIS case history is reported in the hope that the treatment applied—immunization of the patient against her husband's tissues—might be tried in further cases of chorioncarcinoma of placental origin.

The tissues of a mother and child are not compatible; a skin graft from child to mother behaves as a homograft, not an autograft, because of the presence of paternal antigens in the cells of the graft. Since chorioncarcinoma originates from foetal tissue, half the genes in its cells are derived from the father. We considered, therefore, that deliberate immunization of a patient with chorioncarcinoma by her husband's cells might induce or enhance the degree of her tissue incompatibility (homograft immunity) towards cells containing the husband's genes and thereby check or even destroy the tumour. The method of immunization was based on the theory and practice of Medawar and his associates (Gibson and Medawar, 1943; Medawar, 1944, 1945, 1946; Billingham *et al.*, 1956a, 1956b) who showed in experimental animals that pre-treatment of the recipient by either a skin homograft or intradermal injections of blood leucocytes produces an immune response. This was demonstrated by the rapid and violent sloughing of a skin homograft applied subsequently from the same donor.

The present patient, Mrs. E.C., aged 31, mother of a healthy girl aged 1½ years, commenced a second pregnancy in November, 1955. She was admitted to hospital in March, 1956, with a history of heavy bleeding *per vaginam* followed by abortion. The uterus was evacuated, but the curettings were not preserved. She was admitted to a second hospital in late June, 1956, having become increasingly tired and feverish. Investigations showed pyrexia ranging from 100° to 104°, purulent vaginal discharge (pus cells and *Escherichia coli*) and the uterus enlarged to the size of an 8-weeks pregnancy. The haemoglobin concentration was 8·9 g. per cent, the erythrocyte sedimentation rate 34 mm. (Wintrobe) and the male toad pregnancy test was positive using undiluted urine (negative in dilution of 1 in 100).

Persistent vaginal bleeding developed in late July and she was transferred to Hammersmith Hospital at the beginning of August, 1956. On the day of admission the patient felt faint and suffered increasing pain in the lower abdomen; her blood pressure fell from 130/80 to 70/50. Lower abdominal distension, tenderness and guarding and a pulse rate of 100 all added to the clinical picture of considerable intraperitoneal haemorrhage.

She was resuscitated with a transfusion of four pints of blood and an emergency laparotomy was done by Mr. J. Walker. The peritoneal cavity contained fresh and clotted blood. The uterus was enlarged to the size of a 10-weeks pregnancy. Tumour had penetrated from the uterus into the right broad ligament which was ulcerated and bleeding. Total hysterectomy and bilateral salpingo-

oöphorectomy was performed. She was transfused with a further five pints of blood. Three weeks later the patient was started on a course of injections of husband's leucocytes and eight weeks after the operation she was grafted with a one-inch square piece of her husband's skin. Further details of the immunization procedure are given below. The patient recovered satisfactorily and was discharged with no evidence of recurrence.

Summary of the Pathological Findings (G.56/999): Uterus 95×55×25 mm. The fundal endometrium was replaced by friable haemorrhagic tumour which had invaded the myometrium to reach almost to the serosa. The right broad ligament was distended and ulcerated by two haemorrhagic swellings 35 and 25 mm. in diameter. Microscopy shows typical chorioncarcinoma made up of syncytial and cytotrophoblast tumour cells, the latter rich in mitoses. Malignant infiltration of the myometrium and broad ligament is confirmed, growth has invaded the wall of a medium-sized vein in the broad ligament and is seen within the vein lumen.

The patient remained well until November, 1956, when she was re-admitted as an emergency with vaginal haemorrhage of about four pints. The bleeding came from an ulcerated area at the vault of the vagina on the right side. There were two blue nodules in the right vaginal wall below the ulcer each about 1 inch in diameter. She was transfused with 12 pints of blood. Three ovoids of radium were inserted in the vagina and a total dosage given of 4,320 mg. hours. The patient's general condition improved and by April, 1957, the vaginal deposits consisted of a fibrotic mobile mass. These had become impalpable by July, 1957. Serial X-rays of the chest showed no evidence of pulmonary metastases until May, 1957, when small rounded shadows were seen in both lower lobes. These had enlarged by late July, 1957. The patient still felt and appeared perfectly well. A course of 240 Kv. deep X-ray therapy was given during August and the first two weeks of September, 1957, under the supervision of Dr. Lilian H. Walter, to the lower halves of both lung fields. The estimated total tumour dose ranged from 2,500 to 3,500 rads. In October, 1957, the patient continued clinically well, her chest X-ray showed marked diminution in size and intensity of the largest shadow and disappearance of the remainder.

Hogben tests done on undiluted urine at approximately monthly intervals have remained positive throughout. On two occasions they were positive in dilutions of 1 in 10 and 1 in 50 (14th September, 1956 and 23rd May, 1957) and in dilutions of 1 in 100 (20th and 22nd October, 1956). At all other times they were negative in dilutions of 1 in 10.

Immunization Procedure. The patient's blood group was A_1,CDe/cde and the husband's B.cDE/cde. Injections of leucocytes contained in the buffy coat freshly separated from the husband's blood were given into the upper arm and thigh intra-epidermally on each side, the 23rd August, 3rd and 12th September, 1956 and after that subcutaneously on the 29th October, 11th and 20th December, 1956, 1st February, 14th March, 16th April, 15th May and 22nd August, 1957. The earliest injections produced an immediate local reaction which subsided within a week. No systemic reactions were detected. The leucocyte concentrate was made by differential sedimentation of 200 to 300 ml. blood taken into standard disodium citrate dextrose solution (ACD). This yielded 2 to 3 ml. packed leucocytes and platelets with 20 to 30 per cent erythrocytes, which were diluted in a small volume of the husband's plasma for injection.

On 26th September, 1956, Mr. N. Barron, plastic surgeon to Hammersmith Hospital, carried out a group of skin grafts on the patient's thigh. Areas of partial thickness skin grafts about one inch square were taken from the patient, from her husband and from another donor (blood group O) and grafted on to prepared sites. The grafts took successfully and the patient's own skin (autograft) survived. The two homografts disintegrated, the husband's within 12 days, the other donor's within 23 days.

The patient's serum anti-B titre against random group B red cells was relatively low, 1 in 64 to 1 in 256 at room temperature, and showed no rise as a result of the injections. No other blood group red cell iso-antibodies were detected in several trials against a comprehensive genotype panel (tested by Dr. Dorothy M. Parkin). Eight samples of the patient's serum taken between late August, 1956, and July, 1957, were tested by the method of Dausset (1956) for the

presence of leuco-agglutinins. There were no agglutinins to the patient's own leucocytes, weakly positive agglutinins (titre 1 in 1) to the leucocytes of A and O donors and (titre 1 in 1 to 1 in 2) to B and AB donors. However, the titre against the husband's leucocytes varied from 1 in 8 to 1 in 64. Control sera from a panel of untransfused individuals of all the ABO groups showed no leucocyte agglutinins.

The course of injections of husband's leucocytes given prior to the skin grafting may have succeeded in immunizing the patient in that she rejected her husband's skin graft earlier than the other homograft. The development of circulating leucocyte agglutinins was expected in view of the leucocyte injections, but the considerably higher titre found to the husband's leucocytes than to those of group B controls can be considered, together with the skin graft reaction, as evidence that an immunity had indeed developed in the patient against her husband's cells.

Discussion

We have no evidence that immunization to the husband's cells has played any part in the patient's survival to date. In fact, although she is clinically very well at the moment, the pulmonary metastases and persistently positive Hogben test foreshadow a bad prognosis. Spon aneous cures and long survivals of chorioncarcinoma have been recorded. These are exceptional. Obviously the only way of assessing the treatment proposed is by its application to more patients. The low Hogben titre in the urine from the start suggests poor functional differentiation of the tumour, the numerous mitoses in the Langhans cells in the original specimen denote rapid growth. Therefore, the continued survival of the patient in spite of local recurrence and pulmonary metastases, favours the possibility that the tumour has been held in partial check.

Consideration of chorioncarcinoma as a homotransplant brings up the problem of why these tumours do not always induce endogenously an immunity in the patient and thereby lead to their own destruction. Long survivals and spontaneous cures might in fact be the result of such a reaction. Why they do not always do so may well reflect variation from case to case in antigenicity of the tumour and responsiveness of the immune mechanism. Indeed there is a wide range of survival times of skin homografts in humans. These correlate to some extent with the degree of similarity between the blood groups of donor and recipient. Unfortunately, dedifferentiation of tumours is likely to be associated with a loss of antigenic properties and hence loss of vulnerability to immune mechanisms.

Our case was given a prognosis after hysterectomy of three to six months. Her survival to date (October, 1957), of over one year encourages us to think that others might benefit by immunization against the husband's cells. There may well exist examples of chorioncarcinoma in which a boosting of immunity might just tip the balance against the tumour.

Summary

After extirpation of the uterus for chorioncarcinoma a patient was deliberately immunized against her husband's cells by skin grafting and by repeated injections of his leucocytes. It was thought that the resultant transplantation immunity induced or boosted might be effective in checking the growth of residual tumour cells since half of their genes are paternal in origin. The patient has survived the hysterectomy for over a year and is clinically well. However, during this time she developed a local recurrence of growth in the vaginal vault, which was treated with radium, and pulmonary shadows suggestive of metastases, which were treated with X-rays. No claim is made for the immunization treatment in this patient, but the procedure is recorded in the hope that it might be tried in further cases.

Acknowledgments

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Addendum

Mrs. E.C. developed acute pleurisy in November, 1957. The pleural effusion cleared slowly, but by the middle of December, 1957 she developed increasing breathlessness, coughed up blood-streaked sputum and had lost weight. Chest X-rays showed extension of the pulmonary metastases. From January to March, 1958 she was treated with the anti-folic acid preparation amethopterin (methotrexate, Lederle) given in 4 courses, each lasting 5 days (Li *et al.*, 1956). The first day of each course was separated from the previous one by an interval of three weeks. The total dosage of each course was respectively 50, 75, 50 and 75 mg. by mouth.

The lung shadows have cleared and the symptoms are totally relieved. Hogben test on the undiluted urine is negative (April, 1958) and the patient feels well.

Immunity may have helped the action of the anti-folic acid drug in this patient's recovery since amethopterin has not produced a favourable response in males with embryonal or chorioncarcinoma according to a personal communication from Dr. Li of the Memorial Center, New York. It is presumed that in males the chorioncarcinoma cells, which are now accepted to be derived from the host's own cells (Willis, 1953), do not confer a homotransplant type of immunity, in contrast to the trophoblastic cells of the tumour under discussion, which are foetal in origin.

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THE DIAGNOSIS AND SIGNIFICANCE OF MINOR DEGREES OF UTERINE ABNORMALITY IN RELATION TO PREGNANCY

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IN this paper are presented 65 cases of uterine abnormality found in association with pregnancy during an investigation carried out over a period of eighteen months from July, 1954, until December, 1955. The cases were confirmed by hysterography and the skiagrams are presented. A further 28 cases were diagnosed but not confirmed radiologically and yet a further 107 cases are referred to in the text. The probable incidence of the condition appears to be in the neighbourhood of 10 per cent. This contrasts with the previously reported probable incidence of 1 in 78 cases (Way, 1947); 155 cases of "arcuate uterus" in 7,553 deliveries (Falls, 1939); 1 in 1,500 cases (Smith, 1931); 62 in 60,788 cases (Fenton and Singh, 1952). It is possible that the incidence is even higher than suggested, as it is proved in the text of this paper that the majority of women with uterine abnormalities go through pregnancy and labour quite normally, unless some accident in the course of either draws the attention of the obstetrician to the abnormality. In the past, most cases of the condition have been diagnosed accidentally in this manner and a false association between the incidence of the condition and its related dangers to mother and baby has therefore been formed.

It is intended to present and prove certain diagnostic criteria by which the condition can be more easily recognized. In the literature there is a singular lack of emphasis on this aspect of the subject.

The aetiology of abnormalities of the uterus due to anomalies in development or fusion of the Müllerian duct system will not be dealt with in this paper. The embryology and comparative anatomy of their origin has already been well recorded by Jarcho (1946), to whose classic paper the reader is referred. Jarcho's classification of uterine abnormalities will be used in this article as it appears to be the simplest and yet the most truly representative of the condition as found in this investigation.

It is

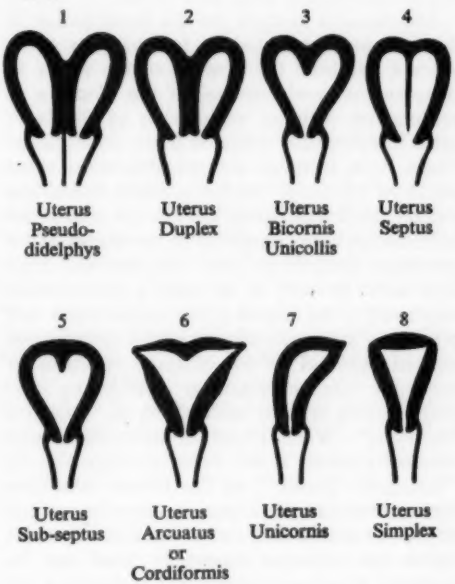

FIG. 1a

The distribution of the 65 proven cases of abnormality in this series according to Jarcho's classification is as follows:

Bicornuate uterus	3
Severe sub-septate or near bicornuate uterus	4
Sub-septate uterus	54
Arcuate uterus	3
Uterus unicornis	1

No examples of the other types of uterine abnormalities were seen by the writer in pregnant women during the period of investigation.

Only 3 cases of arcuate uterus appear in the above distribution of cases. This is misleading as probably a large number of cases classified as sub-septate were, in fact, of the arcuate type. For it is, in my opinion, quite impossible to distinguish between the two types without observing directly the exterior surface of the uterus and few cases in the series were subjected to laparotomy or Caesarean section. This subject will be discussed in more detail later.

The stimulus to carry out the investigation in the first instance arose as follows. For some years it has been the practice of the writer to carry out manual removal of the placenta in conjunction with an exploration of the birth canal in every case delivered under anaesthesia. These have included forceps deliveries, cases delivered by lower uterine segment Caesarean section and breech deliveries. The last mentioned have always been completed by extraction under pentothal anaesthesia after the buttocks have been born. In many of the cases a phenomenon was noted at the fundus of the uterus which had previously been encountered whilst carrying out manual removal of the placenta in cases of *bona fide* retained placenta. This is the condition which will be referred to as "Bilateral Pocketing". When found in association with retained placenta it was often accompanied by "Triangular Spasm". In the former condition the operator has the impression that the cornua of the uterus take the form of small pouches into which the exploring fingers or hand can be inserted. It is best appreciated by running the fingers up along the lateral border of the uterus and when the pocket is reached the hand appears to diverge laterally from the straight line. Sometimes the pocket only appears when steady pressure is applied in the region of the cornu. Occasionally, as with the more marked types of uterine abnormality, a well defined ridge can be palpated at the fundus midway between the two pockets. When the muscle tissue surrounding the entrance to the pockets is in spasm a sphincter-like opening to the pocket is appreciated. When this bilateral cornual spasm is accompanied by sphincteric spasm at the junction of the upper and lower segments at the entrance to the uterine cavity then the picture of "triangular spasm" is complete. In cases of *bona fide* retained placenta, the placenta is often found, either held up in one or other cornu by the cornual spasm, or in the uterine cavity above the entrance spasm. Occasionally it is found held in hour-glass fashion by the spasm.

Bilateral pocketing was found so frequently, particularly when it occurred in conjunction with otherwise apparently normal cases that I was loath at first to diagnose the condition as being due to abnormality of the uterus. I felt that perhaps it was a phenomenon exhibited by the muscle tissue of the contracted and retracted uterus under the action of intravenous ergometrine which each patient had received as a routine measure before the baby's shoulders were delivered. However, many other cases did not exhibit pocketing under the same conditions. Postnatal hysterographic examination was therefore carried out on some of the cases which had exhibited this phenomenon of pocketing and it was found that these did, in fact, display uterine abnormalities of varying degrees. The control cases (those which did not exhibit pocketing) on the other hand showed what I have now come to regard as a normal uterine outline.

I was therefore faced with the conclusion that a large number of women with minor and even advanced degrees of uterine abnormalities were having completely normal confinements and there was nothing unusually obvious in the antenatal signs or in uterine behaviour to attract the attention of the obstetrician to the underlying condition.

Having accumulated a large number of cases of abnormality which were all found by chance it was considered worth while to try to find out if there were not some pointers of diagnosis in the antenatal period which would draw the attention of the obstetrician to the presence of the abnormality.

I began with the diagnostic criteria which, in the past (Falls, 1928, 1939), have been accepted as indicative of the condition and like Stanley Way (1945, 1947) started out purposefully to look for cases.

The diagnostic criteria used were:

(1) Notching, asymmetry and broadening of the fundus of the uterus.

(2) A free head at term in primigravidae in the absence of disproportion and other accepted causes.

(3) Abnormal lies of the foetus in late pregnancy, e.g., transverse and oblique lies and breech presentations.

Diagrammatical records were made in the patients' antenatal notes of the various abnormal uterine shapes and foetal lies encountered and these cases were followed up by uterine exploration and hysterography after delivery. Using these criteria it was found that the diagnosis of uterine abnormalities in the antenatal period proved correct in 76 per cent of cases when these were subjected to hysterography after delivery. But in 24 per cent of cases, on the other hand, the diagnosis was incorrect in that the uterus at hysterography showed either a normal or a "borderline" uterine outline (Tables II and III). It was also found that many cases were passing through the antenatal screen without being detected at all, only to be diagnosed accidentally at exploration of the uterus after delivery. It was therefore obvious that these prenatal diagnostic criteria were not searching enough, either in their diagnostic accuracy, or as aids to identifying the more occult cases in the antenatal period.

By trial and error it was eventually realized that the attitude of the foetus, as opposed to the lie of the foetus *in utero*, was important. In time new diagnostic criteria based on foetal attitude were therefore formulated. These yielded a positive diagnosis of uterine abnormality in the antenatal period of 100 per cent of cases (Tables I and II). It was also found, using these new criteria, that the number of undiagnosed cases discovered accidentally at uterine exploration after delivery fell dramatically.

The revised criteria for diagnosis of uterine abnormalities in pregnancy in what I consider to be their most useful order of importance are shown in Table I. An explanation of the various diagnostic terms and signs employed will be given below.

TABLE I

Diagnostic Criteria in Order of Importance

(1)	Foetal limb flanking with overlie.
(2)	Breech flanking with contralateral limb flanking.
(3)	Foetal limb flanking with fundal notching.
(4)	Broad fundus with fundal notching.
(5)	"Cystic" formation of the uterus.
(6)	A positive Piscacek's sign in early pregnancy.
(7)	A persistent breech presentation.
(8)	Axial deviation of the uterus or foetus without limb flanking.
(9)	Notching or dimpling of uterine fundus only.
(10)	Recurring breech presentation requiring version.
(11)	Free head at term in a primigravida in the absence of disproportion and other accepted causes.
(12)	Recurrent transverse lie.
(13)	Obstetric history, e.g., recurrent abortion, breech delivery.

The most helpful aids to diagnosis are those given at the top of the table, with a 100 per cent diagnostic value attached to the first seven items. It will be seen that the previously accepted signs of the condition have been displaced from their expected place of prominence, with recurrent transverse lie at the bottom of the list. This is because transverse lie, though occurring frequently in cases of abnormality of the uterus, does also occur in uteri which show no abnormality, and therefore it is not a reliable sign. The table has been compiled in this particular order from three sources.

(1) From examination of Table II, which compares the accuracy of the various prenatal signs and post-delivery exploration findings as diagnostic measures in relation to their follow-up hysterographic pictures.

TABLE II

Comparison of Prenatal Signs, Exploration Findings and Certain Recurrent Obstetric Tendencies with Hysterographic Findings

Diagnostic Criteria	Cases giving Positive Hysterographic Diagnosis	Cases giving Negative Hysterographic Diagnosis
Foetal limb flanking with overlie	T, T, L, T, T, 36; L, 34 34 38	Nil
Breech flanking with contralateral limb flanking ..	L, T, T, T	Nil
Limb flanking with fundal notching	36, 36, T, T, T, 34, T	Nil
Broad fundus with notching (heart-shaped uterus)	33, T, 34, 34, 34, 30, 26, 36 34 T 30	Nil
Broad fundus without notching	T, 34, 36 34	35
Fundal notching only	36, 23, 30, 30, L, 33, 32, 33, 28 32 34 34, 36	34, 28, 36 30, 35
Axial deviation of foetus without limb flanking ..	27, 34, L, T 32 36	36, L, T, T, 37 T
Overlie of uterus only	Nil	2 cases
Free head at term in primigravidae	11 cases	2 cases
Recurrent transverse lies in foetus	3 cases	Nil
Cases exhibiting:		
(1) "Cysts" of the uterus	20, T, 36 T	Nil
(2) Piscacek's sign	2 cases	Nil
(3) Recurrent post-partum haemorrhage ..	Nil	2 cases
(4) Recurrent retained placenta	Nil	2 cases
(5) Premature labour	Nil	5 cases
(6) Persistent breech presentation	10 cases	3 cases
(7) Bilateral pocketing of uterus at exploration	42 cases	5 cases

The figures relate to the height of the fundus in weeks at the period of pregnancy at which signs of the condition first presented. In most cases this was the only prenatal occasion on which the patient was seen by the writer. If the patient was seen subsequently and the signs persisted, the fundal heights are columnized in sequence vertically. Cases seen at term are denoted by the letter T and those in labour by the letter L. Each item or column represents a separate case.

(2) From examination of the obstetric history of parous patients with proved uterine abnormalities (Table VI).

(3) From clinical impressions of this series as a whole and from the large number of other cases which have been seen from time to time before commencing the investigation and since its completion. Although I have been unable to follow up these cases their retrospective diagnosis is not in doubt.

EXPLANATION OF DIAGNOSTIC TERMS AND SIGNS

Foetal Limb Flanking

Here the foetal limbs are palpated easily in the maternal flank as represented diagrammatically in Figure 1. If at the same time the limb flanking extends so far laterally that the limbs overlie the maternal flank the sign is referred to as "limb flanking with overlie" (Figs. 2 and 121). Limb flanking with overlie represents a more advanced degree of uterine abnormality than limb flanking without overlie.

Breech Flanking with Contralateral Limb Flanking

If the breech can be palpated on one side of the maternal abdomen and the legs palpated on the other side the sign is referred to as "breech flanking with contralateral limb flanking" or "breech flanking with contralateral limb flanking with overlie" (Fig. 3).

FIG. 1

FIG. 3

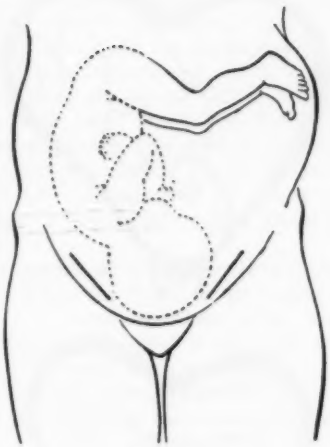

FIG. 2

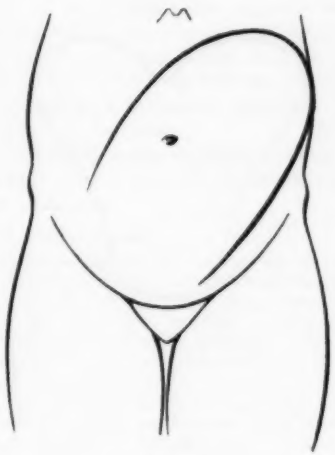

FIG. 4

Axial Deviation

The uterus or foetus or both together may tend to lie obliquely across the maternal abdomen. This is referred to as "axial deviation" (Fig. 4). Reference to the maternal umbilicus is useful in eliciting this sign. If it is accompanied by limb flanking or limb flanking with overlie the diagnosis becomes more positive.

Broadening of Fundus

This is self-explanatory. At or near term the fundus tends to fill out into the maternal flanks on both sides (Figs. 5 and 6).

Notching at the Fundus

This too is self-explanatory (Fig. 6) but the fundus may be asymmetrical (Fig. 7).

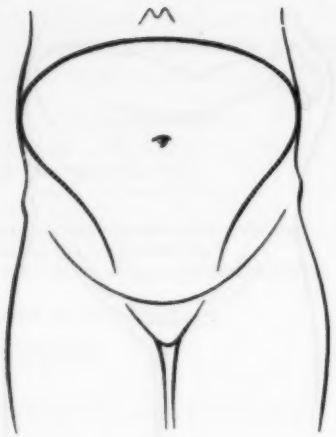

FIG. 5

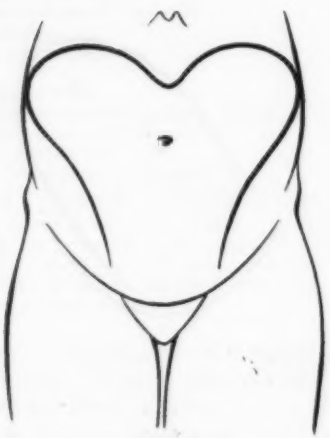

FIG. 6

The diagnosis becomes more definite with a combination of signs, e.g., fundal notching accompanied by axial deviation of the foetus and limb flanking, or by breech flanking with contralateral limb flanking (Figs. 8 and 9).

Cystic Formation of the Uterus

The pregnancy appears to be accompanied by a cystic swelling in the abdomen which

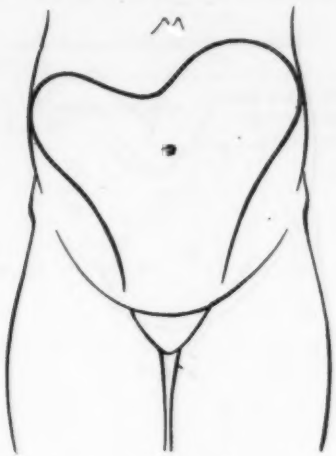

FIG. 7

FIG. 8

FIG. 9

sometimes resembles very closely an accompanying ovarian cyst. The points of difference are:

(1) The "cyst" wall undergoes contraction and relaxation in unison with the uterine contractions and relaxation.

(2) Foetal limbs can usually be palpated or ballotted inside the "cyst" when the uterus is not in tone.

(3) The "cyst" may vary its position or perhaps its obviousness from day to day.

Cystic formation of the uterus will be discussed in more detail later.

I define the normal foetal attitude at or near term as one in which the vertex is presenting and is fixed or engaged in the pelvic brim. The foetus is in a position of complete flexion, with its limbs in close approximation to the trunk. It lies symmetrically central in relation to the maternal umbilicus. The maintenance of this attitude is achieved by the evenly distributed tone of the normal uterus. If the uterus is abnormal the slackening of muscle tone at various points, e.g., at the cornua in a bicornuate or sub-septate uterus, allows extension of the foetal trunk into the pockets of reduced resistance. This gives the flanking limb signs already described. The foetal spine tends to take up a position with the breech pointing into one or other cornu of the uterus (Figs. 8 and 9).

This applies so far to the vertex presenting foetus. When the foetus is presenting by the breech a similar situation arises and axial deviation of the foetal trunk with the head lying in one or other cornu can be very marked. Accompanying signs of broadening and notching of the fundus of the uterus can also occur and one case has been seen with an apparent cyst in one quadrant of the upper abdomen with the foetal head in the other quadrant (Case No. 21577, Figs. 19 and 7).

It was found that the elicited signs become more diagnostic the farther pregnancy had progressed. In the last three to four weeks the elicitation of signs also became increasingly easy, particularly with reference to the foetal attitude.

In the earlier weeks of pregnancy the shape of the uterine outline is all-important. This can sometimes be misleading when the fundus is in the region of the umbilicus. Then the natural dipping of the maternal tissues in this region may give a false positive sign of dimpling of the fundus of the uterus. Uterine mis-shapes in the earlier weeks should be regarded with suspicion and recorded for observation as pregnancy progresses. If in the later weeks they are accompanied by unusual foetal attitudes then the diagnosis becomes more sure.

It should be perhaps stressed that the signs do not always present themselves in an obvious manner as being abnormal. In fact they have already probably been observed many times by the reader without any undue importance being attached to them. But with purposeful elicitation of the signs, keeping the abnormal in view, the examiner becomes increasingly sure of their significance and with continued practice the signs become more and more obvious. The chances of identifying cases increase with the regularity with which the obstetrician sees the patient in the antenatal period, because, as is to be expected, the foetal lie, attitude of the foetus and the outline of the uterus can vary from one observation to the next.

The following cases illustrate the use of the diagnostic criteria as well as presenting other points of interest.

Case No. 23328 (Fig. 40)

Primigravida, aged 26. The patient was seen on three occasions in the antenatal period when the fundal heights were at 27, 32 and 36 weeks respectively. On each occasion the foetus was recorded as lying obliquely towards the right half of the abdomen. (This case was seen early on in the investigation, before the position of the foetal limbs was realized to be important, and so the position of the limbs was not recorded.) The vertex was fixed when the patient was last seen at the clinic. Three days later the patient was admitted in labour. Foetal distress developed when labour had been in progress for thirteen hours and the patient had been 45 minutes in the second stage. A forceps delivery was carried out. The placenta was retained by a uterus exhibiting "triangular spasm". The bilateral pocketing at the fundus was very marked.

The patient, although she did not have any previous referable complaints, died six weeks after delivery from an acute pulmonary infection, secondary to carcinoma of the oesophagus. The uterus was preserved. It showed a typical sub-septate outline on X-ray after the cavity had been filled with opaque fluid. There was a notch on the uterine surface exteriorly. The uterus has therefore been classified as an arcuate uterus (Figs. 40 and 115).

Case No. 24202 (Fig. 41)

Para-1, aged 30. Previous lower uterine segment Caesarean section for inco-ordinate uterine action. The patient was seen for the first time when she was admitted in labour in her second pregnancy. The foetus exhibited the right axial deviation with limb flanking sign. The empty left cornu of the uterus felt hard and resembled a fibroid. Foetal distress developed early in the first stage of labour and a repeat lower uterine segment Caesarean section was carried out. Marked bilateral pocketing was found when the uterine cavity was explored. The external surface of the uterus showed a very shallow depression at the fundus. The patient was unable to report for hysterography until the fourth month after delivery. It was then found that she was pregnant for the third time. Her third baby was delivered by elective lower uterine segment Caesarean section and the patient was sterilized. Bilateral pocketing was again evident at operation. The external surface of the uterus on this occasion was perfectly normal and was photographed (Fig. 116).

Case No. 21660 (Fig. 42)

Para-0, aged 21. The patient was admitted as an incomplete abortion at 12 weeks. At evacuation of the retained products an abnormality in the shape of the interior of the uterus was appreciated with the curette. Hysterography confirmed the bicornuate nature of the uterus. Six months later the patient was re-admitted as a threatened abortion at 13 weeks. The conception sac was passed complete and has been photographed (Fig. 114). It has been moulded to the shape of the uterine cavity. (See also Table VI, addendum, and Fig. 120.)

Case No. 21249 (Fig. 43)

Primigravida, aged 21. Normal antenatal history. The patient was seen at 26 and 36 weeks antenatally. The condition was not diagnosed from the antenatal signs.* The patient had a spontaneous normal delivery at 38 weeks. The placenta was retained in a uterus exhibiting "triangular spasm". At the 6th-week postnatal examination an ovarian cyst was found. Hysterography was carried out. At laparotomy the normal external surface of the uterus was photographed (Fig. 118).

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* Altogether in the 65 cases in the hysterographic series there were 8 cases seen by the writer at one time or another in the antenatal period which were not diagnosed antenatally as having a uterine abnormality. The abnormality was identified only after delivery either at exploration or by hysterography. This makes one believe that there were undoubtedly others which slipped through entirely undiagnosed. Most of those accidentally diagnosed cases appeared at the beginning of the investigation period before it was appreciated how much more important foetal attitude was than foetal lie.

Control Series

These were cases diagnosed at exploration of the uterus as having a normal uterine outline. They include one case which had a spontaneous version of an extended breech at term (No. 22782; Fig. 101). The significance of this will become apparent later in the section dealing with breech presentation. Apart from this last-mentioned case and the 2 cases which subsequently proved to have sub-septate uteri (Table IV) all the control cases had normal antenatal findings with reference to uterine outline, foetal lie and foetal attitude.

Incidence of the Condition

It has already been stated that this investigation was initiated in the first instance to confirm or refute an impression that the high incidence of bilateral pocketing, found in the interior of apparently normal uteri, was due to abnormalities in uterine shape. This having been proved, then an attempt was made to find the true incidence of the abnormality. Besides attempting to elicit signs by which a more accurate diagnosis of the condition could be achieved, other routes of investigation were followed to see if they too could be made to lead in the same direction. It seemed logical to investigate those anomalies of behaviour of function of the uterus which have a recurrent tendency, like premature labour, retained placenta and post-partum haemorrhage. An attempt was made to follow up cases with recurrent history of this type, which had already passed through the hospital statistics. However, it was found quite impossible to achieve a satisfactory follow-up of these cases. For the most part, they were either not willing to be subjected to X-ray or were unable to attend for examination. Of those who attended some were already again pregnant and in others there were gynaecological contra-indications to carrying out the investigation. It therefore fell to the lot of those delivered during the period of the investigation to provide the material for follow-up. The findings in the few cases with recurrent histories which were investigated are shown in Table II. The results were anything but encouraging. This line of investigation was therefore not pursued.

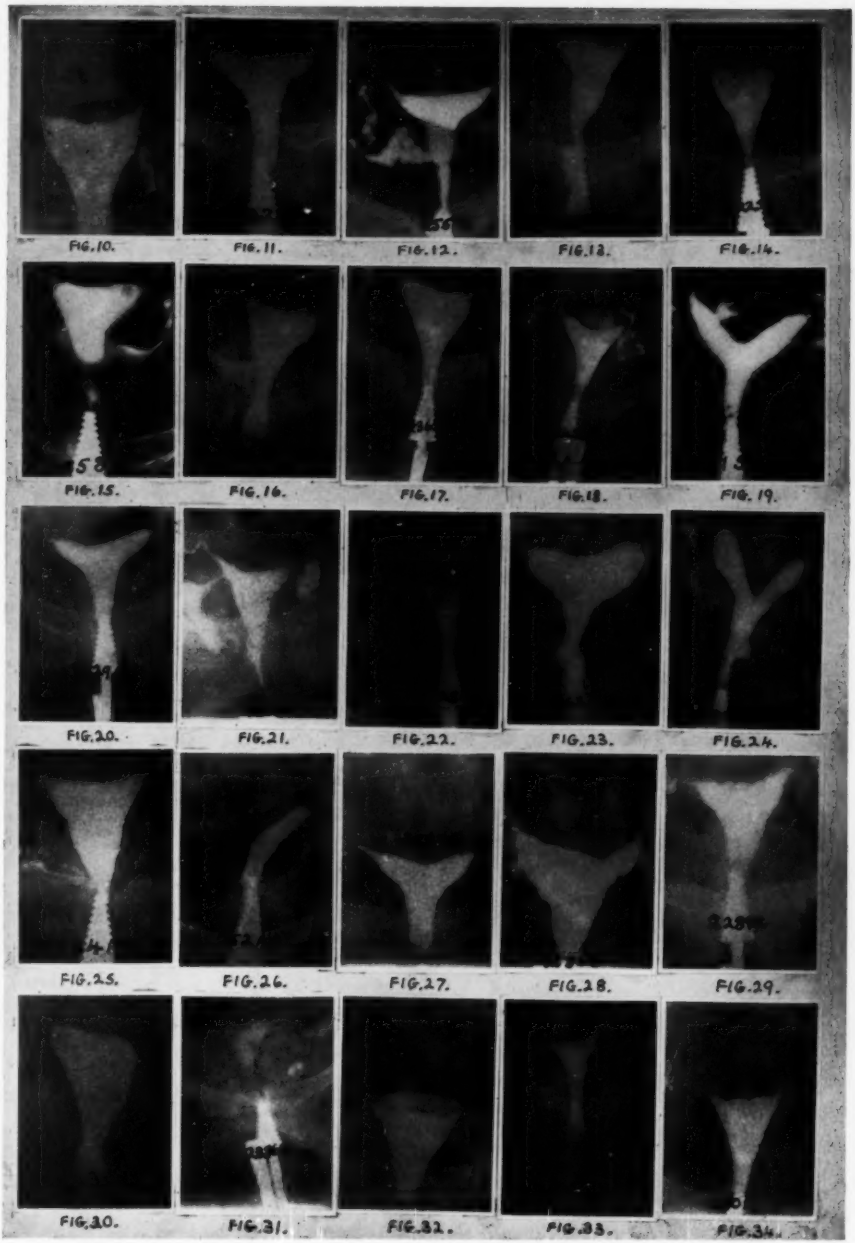
FIG.10.
FIG.11.
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FIG. 45. FIG. 46. FIG. 47. FIG. 48. FIG. 49.

FIG. 50. FIG. 51. FIG. 52. FIG. 53. FIG. 54.

FIG. 55. FIG. 56. FIG. 57. FIG. 58. FIG. 59.

D.H.

FIG. 60. FIG. 61. FIG. 62. FIG. 63. FIG. 64.

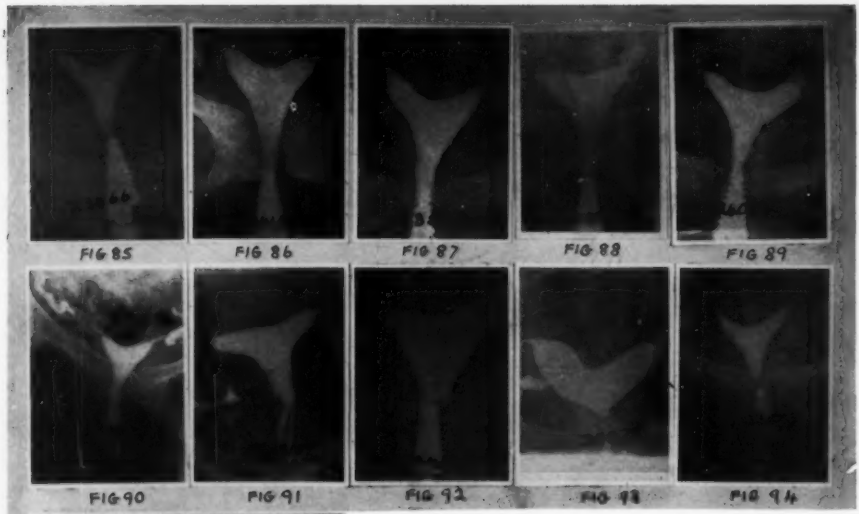
FIG. 65. FIG. 66. FIG. 67 FIG. 68 FIG. 69

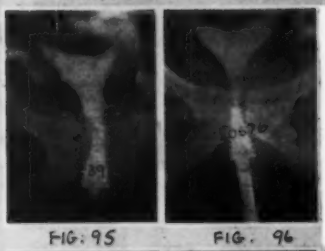
FIG. 70. FIG. 71. FIG. 72. FIG. 73. FIG. 74.

FIG. 75. FIG. 76. FIG. 77. FIG. 78. FIG. 79.

FIG. 80. FIG. 81. FIG. 82. FIG. 83. FIG. 84.

D.H.





CONTROL CASES

FIGS. 97–113

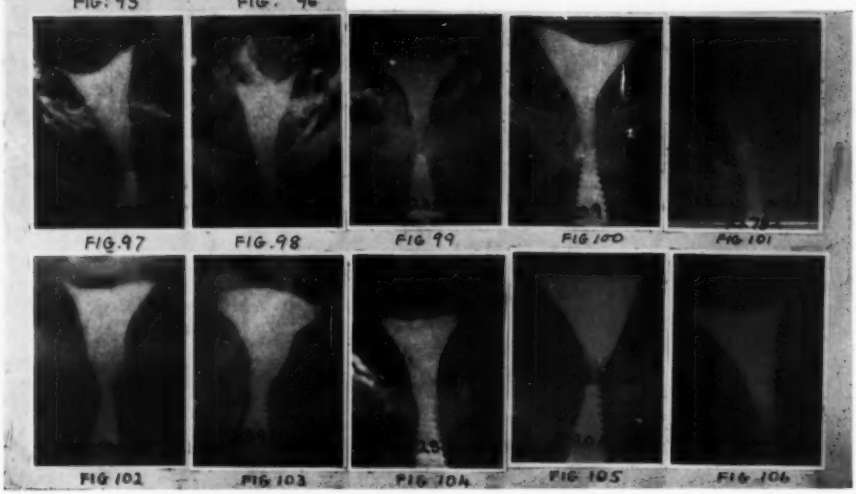


FIG. 107. FIG. 108. FIG. 109.

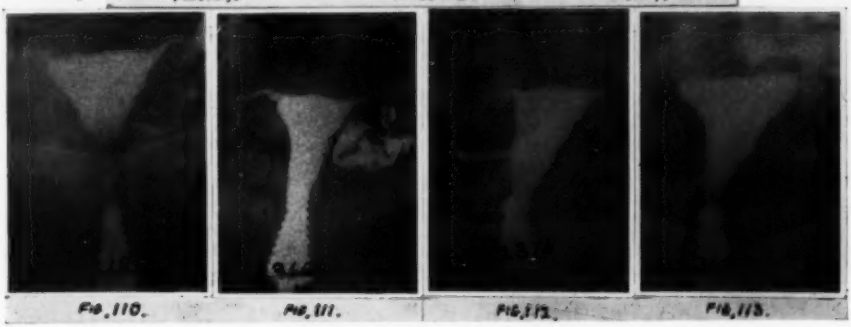


FIG. 110. FIG. 111. FIG. 112. FIG. 113.

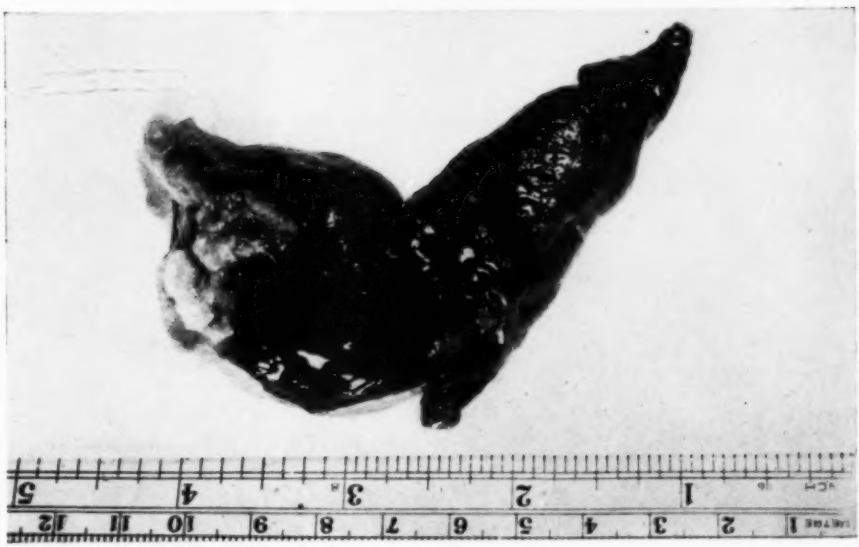


FIG. 114

Fig. 115

FIG. 116

FIG. 117

FIG. 118

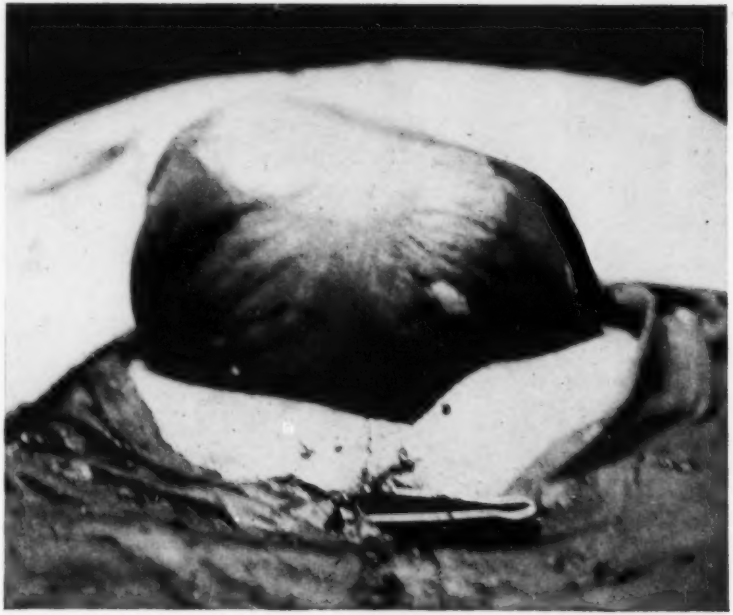


FIG. 119

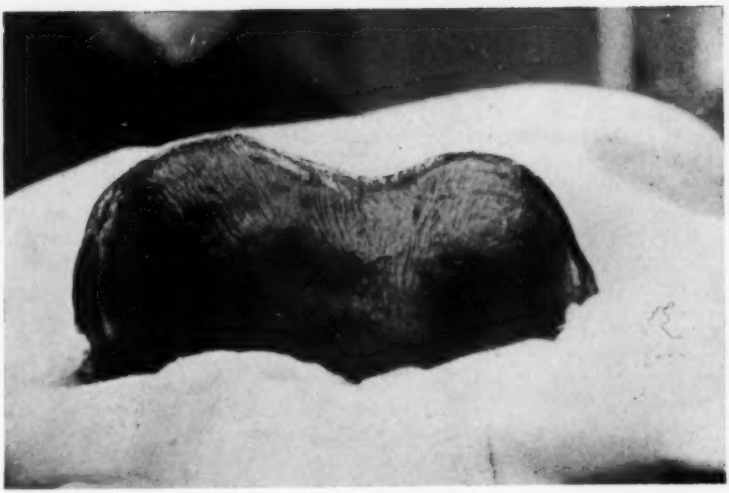


FIG. 120

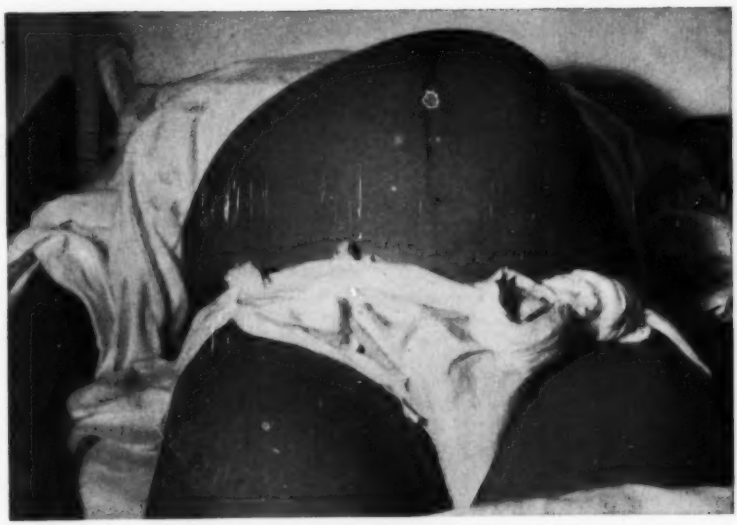


FIG. 121
Showing "limb flanking with overlie" and cystic formation of the uterus.

Altogether in the series a hysterographic examination was carried out on 111 cases. Of these, 85 were previously diagnosed either at exploration of the uterus or antenatally as having an abnormal uterus. Nine were cases who had had a recurrent history of malfunction of the uterus and the remaining 17 cases were controls (Table III). Two cases had a second X-ray examination carried out some months after the first picture to see if the X-ray outline of the uterus had changed in any way with continued involution. There was no change (Figs. 52, 53, and 55, 56).

At the beginning of the investigation all cases which had been diagnosed from the antenatal findings as having probable uterine abnormalities were subjected, where possible, to an exploration of the birth canal as well as hysterography. As the investigation proceeded and the diagnostic criteria became more accurate in their application, exploration of the uterus was dispensed with as a routine measure and most cases were then allowed to follow the normal procedure of the delivery wards and invited to return for hysterography. When possible, hysterographic examination was carried out at 6 weeks after delivery. This period was chosen because:

(1) It was found easiest to get the patient to attend when the hysterographic examination was combined with the routine sixth-week postnatal examination.

(2) The patient was less likely to be menstruating or pregnant again at this time.

(3) Involution is said to be complete at this stage.

Although the sixth-week period after delivery was aimed at, a large number of patients was not X-rayed until 10 or 12 weeks or even longer afterwards. This did not appear to make any appreciable difference to the expected findings on X-ray (Table VI).

It was found that the patient who was subjected to the most interference during her stay in hospital was the most likely to return for further examination, and that, conversely, the majority of those who failed to report for hysterography came from the group whose diagnosis was made antenatally, and allowed to follow the normal routine of the labour wards.

Of those who failed to attend, or were not X-rayed because of previous exposure to X-rays, or in whom there was a gynaecological contra-indication to carrying out hysterography, 28 cases were diagnosed either by exploration of the uterus, or by the "100 per cent" diagnostic criteria, or by both methods, as having abnormal uteri. A further 36 cases had possible uterine abnormalities, but as these could not be confirmed either by exploration or by X-ray, and as the antenatal signs exhibited by them were not of the "100 per cent" variety, they have been excluded entirely from the investigation, but for statistical purposes, are referred to. Yet a further series of most probable uterine abnormalities is derived from the 87 cases of persistent breech deliveries carried out at the hospital during the period of investigation and of which 13 have already been included in the 85 pre-diagnosed cases referred to above. Three of these had normal hysterographs. The breech cases make a study in themselves and are discussed separately.

Altogether there were, therefore, 200 proved, probable and possible cases of uterine abnormality seen during the period of the investigation. There were in the hospital during this period 2,088 deliveries from which the cases were diagnosed. The incidence of the condition appears therefore to be in the neighbourhood of 10 per cent.

Hysterographic Technique

The patient was prepared for investigation in the usual manner. The uterus was filled with Neo-Hydriol solution under direct X-ray screen visualization. The uterus was manipulated by pulling down on the volsella forceps until the best outline of the fundus could be realized and then, just as the Fallopian tubes commenced to fill with opaque fluid, an immediate picture was taken, using the same under-couch X-ray tube and dispensing with the Bucky plate.

Several pictures showed extravasation of the opaque fluid into the pelvic veins, e.g., Figures 38, 41, 47, 51 and 59. Since this phenomenon is in no way related to the investigation under

review no further reference will be made to it. There were no complications in any of the patients investigated.

It will be seen from Table III and from the analysis of the misdiagnosed cases in Table IV that the most accurate diagnostic criteria are those which relate to foetal attitude, since the mistakes amongst the abnormal uteri are associated, without exception, with those cases where the diagnosis was made on the old criteria of foetal lie and uterine shape.

The apparent vagrancies of bilateral pocketing as a sign of uterine abnormality would require explanation as mistakes due to it appear in both the abnormal and the control series (Tables II and IV).

In support of it I point out that the mistakes in the abnormal series relate only to borderline cases and in the control series to borderline and mild cases of abnormality. Misdiagnoses occur simply because mildly abnormal uteri, if not well contracted and retracted under the

TABLE III

Statistical Survey of Cases Investigated

Total number of *potentially* abnormal cases			203
Cases diagnosed by "100 per cent" criteria, but not X-rayed	28		
Cases with possible uterine abnormalities, but not X-rayed	36		
Cases with probable uterine abnormalities from breech series	87		
Total number of cases X-rayed			111
Cases diagnosed as abnormal either at exploration or antenatally (including 13 breech presentations)	85		
Cases with recurrent anomalies of uterine function	9		
Control cases	17		
Total number of abnormal uteri found on X-ray			65
Positive diagnostic accuracy: 76·6 per cent.			
1. *In Vertex Presenting Foetuses and Abortions:*			
Number of cases X-rayed			72
Number of abnormal uteri			55
Diagnosed prenatally	34		
Diagnosed at exploration	18		
Diagnosed at evacuation of incomplete abortion	4		
Bicornuate uteri		3	
Severe sub-septate uteri		2	
Sub-septate uteri		47	
Arcuate uteri		3	
Borderline uteri, ? normal, ? sub-septate (? misdiagnosed)		7	
Normal uteri (misdiagnosed)		10	
2. *In Breech Presenting Foetuses:*			
Number of cases X-rayed			13
Number of abnormal uteri			10
Bicornuate uteri	0		
Severe sub-septate uteri	2		
Sub-septate uteri	7		
Arcuate uteri	0		
Unicornuate uteri	1		
Borderline, ? sub-septate, ? normal (? misdiagnosed)	1		
Normal uteri (misdiagnosed)	2		
3. *In Control Cases:*			
Number of cases X-rayed			17
Number of normal uteri			13
Sub-septate uteri	2		
Borderline uteri, ? normal, ? sub-septate (? misdiagnosed)	2		
Positive diagnostic accuracy: 76·5 per cent.			

TABLE IV

Analysis of Cases Misdiagnosed in Table III

I. Vertex Presenting Foetuses:

A. Borderline uteri (7): Criteria of diagnosis used:

Case No.	
15123 (Fig. 10)	Axial deviation only without leg flanking in labour.
2277 (Fig. 11)	Axial deviation only without leg flanking at 37 weeks.
25506 (Fig. 12)	Fundal dimpling only at 34 weeks in a twin pregnancy and bilateral pocketing at exploration.
21489 (Fig. 13)	Mild degree of bilateral pocketing at Caesarean section for severe toxaemia.
22259 (Fig. 14)	Bilateral pocketing after forceps delivery.
18585 (Fig. 15)	Slight dimpling at fundus at exploration after forceps.
23748 (Fig. 16)	Bilateral pocketing at exploration.

B. Normal uteri (10): Criteria of diagnosis used:

14371 (Fig. 30)	Bilateral pocketing at Caesarean section.
23868 (Fig. 31)	Broad fundus only at 38 weeks (not appreciated at term).
24686 (Fig. 32)	Fundal dimpling only at 28 weeks.
24787 (Fig. 33)	Fundal dimpling only at 36 weeks.
8801 (Fig. 34)	Fundal dimpling only at 35 weeks.
3907 (Fig. 35)	Fundal dimpling only at 30 weeks.
25289 (Fig. 36)	Axial deviation only without limb flanking at term.
23263 (Fig. 37)	Axial deviation only without limb flanking at term.
23916 (Fig. 38)	Axial deviation only without limb flanking at term.
1192 (Fig. 39)	Axial deviation only without limb flanking at term.

II. Breech Presenting Foetuses:

A. Borderline uteri (1):

23635 (Fig. 17)	Bilateral pocketing at exploration.

B. Normal uteri (2):

16236 (Fig. 22)	Premature delivery at 32 weeks. Previous premature delivery at 34 weeks.
24109 (Fig. 25)	Previously undiagnosed breech presentation—unilateral pocketing at placental site.

III. Control Cases:

A. Borderline uteri (2):

23694 (Fig. 97)	Retained placenta, contraction ring at junction of upper and lower uterine segment. No pocketing.
23467 (Fig. 98)	Retained placenta with post-partum haemorrhage. No spasm. On manual removal a small pocket was palpated at one cornu which at the time was taken to be due to placental siting in this area.

B. Sub-septate uteri (2):

23903 (Fig. 99)	Free head at term in a primigravida. Forceps delivery after 26 hours in labour. Exploration of poorly contracted uterus—no pocketing—uterus diagnosed as normal.
22976 (Fig. 100)	Primigravida—external cephalic version at 32 weeks and 34 weeks—legs flexed. Free head at term. Forceps delivery. Exploration of poorly contracted uterus—no pocketing—uterus diagnosed as normal.

action of an oxytocic drug, may fail to give the pocketing sign.

The elicitation of the sign of bilateral pocketing requires practice, without which the sign, as a diagnostic measure, obviously has its limitations. This has been proved by finding on X-ray marked degrees of uterine abnormality in cases which other observers had, at exploration, passed as normal.

It is obviously impossible to state categorically where the normal hysterographic outline becomes abnormal. Particularly is this so when

one considers how completely normal cases of even gross uterine abnormality are in their behaviour. So far we have had no definite standards of behaviour to distinguish the normal uterus from the abnormal. The literature to date reflects this and writers are therefore particularly varied in their definition of the normal hysterographic outline (Davis, 1939; Goldberger *et al.*, 1950; Brocq, 1954). Both Goldberger and Brocq present hysterographic pictures of "normal uterine outline" which in my experience of uterine exploration and follow-up hysterography I would classify as sub-septate.

I am satisfied that the finding of bilateral pocketing in uteri after delivery is a most reliable differential on which to base standards of uterine behaviour and in this paper it is the yardstick which I have employed to distinguish the normal from the abnormal. I do not consider that the pocketing effects found after delivery can be attributed to the effects of oxytocic drugs, as they are also present in the contracted uterus of the patient who has not received oxytocic drug therapy. I believe that oxytocics only make the pocketing effects stand out more clearly. The normal uterus does not exhibit pocketing effects nor can these be induced by the administration of oxytocic drugs. The X-ray photographs (Figs. 97–113) in the control series are presented therefore as uteri having normal hysterographic outlines. All these uteri were explored after ergometrine had been administered intravenously to the patient and in none of them was bilateral pocketing encountered.

Behaviour and Outcome of Cases

No useful purpose can be achieved by examining the behaviour of those cases which exhibited the grosser types of deformity apart from the others, as it was found that all cases were equally unpredictable in their behaviour. The following table (Table V) is a summary of the outcome of the 65 proven cases of uterine abnormality. The behaviour and outcome of the 10 cases of breech presentation included in these 65 cases is dealt with in more detail separately.

Table V

Outcome of 65 Proven Cases of Uterine Abnormality

Number of forceps deliveries	12	
Number of cases treated by lower uterine segment Caesarean section	10	inco-ordinate action (4) foetal distress placenta praevia obstetric history two previous Caesarean sections large breech placenta praevia + breech
Number of retained placenta	12	(5 cases following forceps deliveries)
Number of cases exhibiting inco-ordinate uterine action	8	Caesarean section (4) Pitocin-pethidine drip (2) (1 forceps, 1 normal) forceps (2)
Number of cases with associated placenta praevia	2	
Number of cases exhibiting transverse lie in pregnancy	3	internal version Caesarean section (foetal distress) normal delivery
Number of cases with post-partum haemorrhage	2	
Number of cases exhibiting free head at term	11	
Number of cases ending in abortion	5	
Number of cases with completely normal confinements	24	
Number of stillbirths	3	prolapsed arm gross foetal deformities (2)
Number of cases delivered vaginally with breech presenting	8	

TABLE VI
Obstetric History of 23 Parous Patients

No.	Parity	Outcome of Previous Pregnancies	Present Pregnancy		X-ray at Weeks	Figure No.
			Antenatal Signs	Outcome		
20880	1	Abortion of 14 weeks.	Limb flanking with overlie.	Normal.	11	51
23595	1	Abortion, 12 weeks.	Axial deviation with fundal notching.	Normal.	7 and 28	52, 53
23613	2	Normal.	Not seen.	Prolapsed arm. Internal version. Stillbirth.	7 and 40	55, 56
21660	1	Abortion, 12 weeks.	—	Abortion 13 weeks (see photo Fig. 114, addendum and Fig. 120).	6	42
11017	2	1. Normal. 2. Abortion, 12 weeks.	Heart-shaped uterus 24 weeks. Right axial deviation 34 weeks.	Type IV placenta praevia L.U.S.C.S.	12	54
14585	2	1. Normal. 2. L.U.S.C.S. (foetal distress).	Axial deviation with limb flanking with overlie.	Normal.	6	57
16086	1	Normal.	Axial deviation.	Normal.	10	58
16356	2	1. Normal. 2. C.S. (shoulder presentation).	Broad fundus. Breech.	Type III. Placenta praevia L.U.S.C.S.	11	23
12518	1	Abortion, 10 weeks.	Free head at term.	Normal delivery. Retained placenta.	8	46
25746	2	1. Normal—died. 2. Breech—stillbirth.	Fundal dimpling 30 weeks. Limb flanking with overlie 36 weeks.	L.U.S.C.S. (history).	10	59
1079	5	Normal.	Fundal notching 30, 32 and 34 weeks.	Normal.	8	60
24202	1	1. L.U.S.C.S. (inco-ordinate action).	Limb flanking with fundal notching.	Inco-ordinate action L.U.S.C.S.	6	41
1915	2	1. Normal. Retained placenta. Post-partum haemorrhage. 2. Normal.	Fundal dimpling 30, 34. Axial deviation at term.	Normal.	6	61
2520	1	Normal.	Fundal notching, 22 weeks.	Abortion.	7	62
6944	2	1. Forceps. Retained placenta. 2. Abortion, 22 weeks.	—	Abortion, 17 weeks.	12	63
8636	1	Breech.	Limb flanking with overlie.	Normal.	72	64
11251	2	1. Abortion, 10 weeks. 2. Normal.	Not seen.	Normal delivery. Retained placenta.	7	65
10053	3	1. Forceps. 2. Abortion, 10 weeks. 3. Abortion, 12 weeks.	—	Abortion, 9 weeks.	6	66
25808	2	1. Forceps. 2. Normal.	Breech (Hydrocephaly).	Breech extraction.	16	28
22946	1	Abortion, 10 weeks.	Not diagnosed.	Inco-ordinate action. Pitocin-pethidine drip. Normal delivery.	8	44
22896	1	Normal.	Fundal notching, 32 weeks.	Normal.	8	67
23959	1	Normal.	Fundal notching, 38 weeks.	Normal.	6	68
3508	1	Forceps.	—	Abortion, 12 weeks.	9	69

The 12 forceps deliveries were in primigravidae and were performed for delay in the second stage. Three of them were associated with inco-ordinate action of the uterus. One of the latter required pitocin-pethidine drip infusion intravenously to achieve full dilatation of the cervix.

Five of the 12 cases of retained placenta followed forceps deliveries. The indication for manual removal in these cases was the palpation of a contraction ring at the junction of the upper and lower segments on vaginal examination at the conclusion of the second stage of labour. The contraction ring was almost certainly stimulated by the manipulation incident upon delivery in association with the ergometrine given to the patient intravenously on delivery of the anterior shoulder.

In the 65 proven cases of uterine abnormality there were 23 parous patients. A summary of the obstetric histories of these 23 cases is given in Table VI.

To summarize, these 23 patients had 61 pregnancies between them with the complications shown in Table VII.

TABLE VII

	No. of Cases	Per cent
Abortion	15	24·5
Forceps	3	4·9
Caesarean section	7	11·5
Retained placenta	4	6·5
Transverse lie	2	3·3
Post-partum haemorrhage ..	1	1·6
Breech presentation	4	6·5
Placenta praevia	2	3·3
Inco-ordinate uterine action ..	1	1·6

Thus, *in toto*, the 65 proven cases of abnormality had between them 114 pregnancies with the complications shown in Table VIII.

In the literature to date this has been the usual way of presenting the complications due to uterine abnormalities and a comparative table published by Stanley Way (1947) giving the complication rate in 37 cases of uterine abnormality (78 pregnancies) is as shown in Table IX.

TABLE VIII

	No. of Cases	Per cent
Abortion	15	13·1
Forceps	12	10·5
Caesarean section	13	11·4
Retained placenta	14	12·3
Transverse lie	4	3·5
Post-partum haemorrhage ..	3	2·6
Placenta praevia	2	1·8
Inco-ordinate uterine action ..	8	7·1
Free head at term	11	9·0

TABLE IX

	No. of Cases	Per cent
Transverse lie	21	27
Abortion	19	26
Retained placenta	12	15
Breech	7	9
Premature labour	7	9
Placenta praevia	5	5
Prolapse of cord	4	5

(The corresponding figures in the present series are lower only because the number of diagnosed cases having a normal outcome to their pregnancies is higher.)

But such tables give a completely false impression of the importance of, or dangers attached to, pregnancy occurring in the malformed uterus, as a large number of the cases in both Way's and the author's series (as they are expressed here) were diagnosed by chance. To get a clearer picture of the probable outcome of pregnancy when it is associated with an abnormality of the uterus, one should examine either cases which have been diagnosed *before* any complication of pregnancy has arisen to draw the attention of the obstetrician to the abnormality or the obstetric history of parous patients with known uterine abnormalities (Tables VI and VII). In this series there were 32 cases in primigravid patients with vertex-presenting foetuses which had been successfully diagnosed from the antenatal findings as having a uterine

TABLE X

		Cases	A Percentage	B Corrected Percentage
Forceps deliveries	7	twins—delay delay (4) foetal distress inco-ordinate action	21·3	14·5
Retained placenta	4	(3 associated with forceps)	12·5	7·3
Inco-ordinate action	2		6·1	3·7
Post-partum haemorrhage	1		3·1	1·8
Transverse lie	2		6·1	3·7
Placenta praevia	1		3·1	1·8
Free head at term	5		15·6	10·9
Normal confinements	21		65·6	72·7
L.U.S.C.S.	4	foetal distress placenta praevia inco-ordinate uterine action postmaturity	12·5	12·7

abnormality. The obstetrical outcome of these 32 cases is as shown in Table X, Column A.

The forceps delivery and Caesarean section rate is about double the incidence in the hospital as a whole. The association of retained placenta with forceps delivery has already been commented upon. It should be noted particularly that there was only one case of retained placenta following an otherwise normal confinement.

But this table too can be misleading in the interpretation as the cases it refers to are, to a certain extent, selective; they were the 32 cases which returned for hysterography, and, as it has already been observed, it was the patients who had had most surgical interference who were most likely to attend for X-ray. In addition to the 65 cases of hysterographically proved abnormality, there were the further 28 cases with vertex presenting foetuses in which an X-ray was not obtained, and these have already been referred to. Twenty-three of these 28 cases were also in primigravidae and were diagnosed in the antenatal period from the "100 per cent" diagnostic criteria, as having uterine abnormalities. Of these 23 cases, 19 had normal confinements. Of the remaining 4, 1 had a forceps delivery for delay in the second stage and 3 had lower uterine section Caesarean section operations performed, for which the indication, in two, was foetal distress, and, in the third, inco-ordinate uterine action. In the last case the patient started labour with a free head.

The corrected itemization of the various complications is shown in Table X, Column B. It is likely that these figures could be reduced still further by a more careful antenatal assessment of patients, for I am sure that there must be many cases who have completely normal confinements, who slip undiagnosed through even the most assiduous antenatal scrutiny.

BREECH PRESENTATION

DeLee and Greenhill (1947) give the incidence of breech delivery as 3 per cent, Vartan (1945) cites 117 breech deliveries in 3,875 total births, again an incidence of 3 per cent. Of these 117 cases, 32 can be excluded in that they comprise the "unheralded remnant", that is, the premature, the macerated, the second twin, etc., so that the remainder, which represents an incidence of 2·2 per cent is a more true assessment of the incidence of breech deliveries. In the 18 months during which this investigation was carried out there were 106 breech deliveries at St. David's Hospital. The unheralded remnant amongst those was 19 cases. During this period also 2,936 cases were supervised at the antenatal clinics in the area, so that the incidence of breech delivery in the period under review is 2·9 per cent.

In Table VII the incidence of breech delivery amongst 23 parous patients with uterine abnormality is 6·5 per cent; the corresponding figure in Way's series is 9 per cent, so that the incidence of persistent breech presentation in association with uterine abnormality is probably 2 to 3 times the incidence in any general hospital series of breech deliveries. Falls (1939) expresses the incidence as 16·2 per cent of his presented cases, and Fenton and Singh (1952), 14·8 per cent of theirs. But these latter figures, for the most part, represent the chance discovery of breech presentation in association with uterine abnormality and are therefore not acceptable.

In this series there were 10 cases of breech presentation with positive hysterograms included in the 65 cases of proved uterine abnormality presented, but I have avoided purposely in the text expressing these as a percentage of the total, as has been the practice of most writers in the past.

Breech presentation in relation to uterine abnormalities is discussed separately from the cases in which the foetus presented by the vertex. This is because there is reason to believe that breech presentation in itself is an indication of uterine abnormality. This is particularly true if the foetal legs are extended. The 10 cases of uterine abnormality were discovered in the 13 cases of breech delivery in which hysterography was carried out (Figs. 17–29 inclusive). For the most part, these were the only cases out of the 87 breech deliveries who reported back for X-ray examination, though there were other cases, as has already been explained, in which X-ray examination was either not feasible, or was considered inadvisable. The cases were investigated in the first instance, because the breech was presenting, and not because an abnormality of the uterus was found accidentally on exploration of the uterus after delivery. The high incidence of proved uterine abnormality in association with the presenting breech is supported clinically by the almost monotonous regularity with which bilateral pocketing of the uterus was found in association with breech presentation in general over a large number of breech deliveries before the investigation was instituted, and since its completion. Extended breech presentation is now, in my judgment, almost diagnostic of uterine abnormality.

All 13 cases of breech presentation in the series had a uterine exploration carried out as well as the follow-up hysterogram and the results are given in Table XI.

In 8 cases the placental site was defined. In 6 of these the site was in one or other cornu of the uterus. The placental site in the other cases was not defined because they occurred at the beginning of the investigation, and it was not realized at that time that the actual placental siting was of much significance.

In 9 of the cases the baby had extended legs. The 3 cases of flexed legs occurred in a case of severe sub-septate uterus, a unicornuate uterus and in a case associated with placenta praevia.

TABLE XI

Position of Legs	Position of Placental Site	Type of Uterine Abnormality (X-ray)	Remarks
Extended	?	Sub-septate	
Extended	Cornual	Normal	
Extended	Cornual	Sub-septate	Hydrocephaly
Extended	?	Severe sub-septate	
Extended	?	Sub-septate	
Extended	Posterior wall	Borderline	
Extended	Fundal	Sub-septate	
Extended	Cornual	Sub-septate	Hydrocephaly
Extended	Cornual	Sub-septate	
Flexed	Cornual	Severe sub-septate	
Flexed	?	Sub-septate	Placenta praevia
Flexed	Cornual	Unicornuate	
?	?	Normal	Premature 32 weeks

It is considered that the association of extended legs, cornual placental implantation and uterine abnormality is very significant in the explanation of persistent breech presentation. It is interesting to surmise which one of them, or combination of them, is the dictating factor. Both Vartan (1940) and Stabler (1947) have drawn attention to the high association of extended legs with breech presentation. Vartan postulates that the presentation is due to the splinting action of the foetal legs, whilst Stabler thinks that a breech presentation persists because, when the legs are extended, the baby cannot kick itself away from the fundus of the uterus as it can from the pelvic brim when the legs are flexed. Vartan found that in 37·3 per cent of his breech presentations the legs were extended; Stabler's figures are as high as 90 per cent for breech presentation in primigravidae.

Stevenson (1949), in an X-ray study of placental siting, has shown that the site was cornual in every case of breech presentation in 76 cases. He claimed a 100 per cent diagnostic accuracy in visualization of the placenta as proved by carrying out an exploration of the uterus after delivery. Whitehead (1953) repeated the investigation and found that, of 86 cases of persistent breech, 60 cases had cornual implantation of the placenta, and, in 90 cases of cornual implantation of the placenta, the legs were extended in 58, flexed in 21, and in the remainder there was one leg flexed and one extended. Both authors therefore assume that there is a correlation between breech presentation and cornual placental implantation, though Whitehead admits that other factors like foetal attitude and abnormalities of the uterus must also play a part.

Clinical impression certainly supports the high correlation between breech presentation and cornual placental siting. However, there is the equally high correlation of uterine abnormality with extended breech presentation to be fitted into the picture. How important is the uterine abnormality *per se* in the production of the breech presentation? But then, also, how important are extended legs or cornual implantation *per se* in the production of breech presentation? So far, from Vartan's and Stabler's investigation, it would appear that there is some definite association between the extended attitude and the presentation, otherwise they would not occur so often in association with each other. Similarly we might say from Stevenson's and Whitehead's findings that cornual implantation and breech presentation bear an important association. But surely the fact that two apparently isolated phenomena can be used to prove the dependence of an occurrence which is common to both of them invalidates the strength of the argument for each. A conclusive test for either argument would be to find out how often extended legs occur and how often the placenta is cornual in vertex presenting babies without obviously a breech presentation resulting. An attempt was made to do this. The X-rays of 100 vertex presenting foetuses of 36-weeks maturity upwards were inspected. These were taken at random from the files from the section corresponding to the period of investigation. The period chosen assumes that most of the X-rays of possible cases of uterine abnormality had already been "weeded out" since the already known cases had been removed from the files, so that the X-rays remaining were of foetuses in presumably normal uteri. The foetal legs were extended in 34 cases. Four cases were excluded in which one leg was extended and one flexed.

At the same time it was found in 34 cases of vertex presenting babies in the series which had an exploration of the uterus carried out, that the placenta was sited cornually in 24 cases. In the remainder the position of the placental site was not defined.

From these findings, therefore, it appears that extended legs, even in vertex presentations, are very common and therefore by themselves cannot be held responsible for breech presentation. Also it seems that a cornual implantation of the placenta is just as common in cases of uterine abnormality when the foetus presents by the vertex as it is when the breech presents, so it too, *per se*, cannot be held responsible for the breech presentation. We are, therefore, left with the uterine abnormality itself as the common denominator. But the uterine abnormality *per se* cannot be the cause, otherwise the incidence of breech presentation would be higher than the recorded 6·5 per cent. Let us

assume that it is the extended attitude of the foetus in association with the uterine abnormality that is responsible. In order to test the strength of this hypothesis, inspection was made of the X-ray pictures taken during pregnancy of 22 vertex presenting foetuses of patients in the series who had proved uterine abnormalities. The pictures had been ordered by different observers for various reasons unconnected with the presence of a possible uterine abnormality. Of these only 2 cases had extended legs, i.e., 9·0 per cent. This contrasts with the incidence of 34 per cent extended legs in presumably normal uteri and suggests that, when the foetal legs are extended in cases of uterine abnormality, the baby tends to present by the breech. The fact that the placenta is also cornual appears to be only an incidental finding, dependent on the fact that it tends to be cornual anyway in cases of uterine abnormality. This perhaps is not unexpected, because, if it were fundal in situation, it would tend to separate prematurely. No doubt this is what happens in many cases of abortion and helps to explain the high incidence of abortion in these cases.

Unfortunately the number of cases involved in this hypothesis is too small to be taken as serious proof of what appears clinically to be an established fact in the mind of the writer. However, the findings, as far as they go, are suggestive and it is inferred from them most strongly that it is the extended attitude of the foetus in relation to the uterine abnormality that is responsible for the persistent breech presentation.

The actual mechanism of production of the presentation appears to be purely mechanical. Vartan has shown that, in one in every four pregnancies, the foetus presents as a breech at some time or another, and the natural tendency is eventually towards spontaneous version to a vertex presentation around the 34th week or sometimes nearer term. In the malformed uterus as the growing foetus eventually reaches the optimal size (34th week onwards), spontaneous version becomes increasingly more difficult, because the foetal head gets caught up in one or other sacculation at the cornua of the uterus, and the extended attitude of the foetus prevents sufficient flexion of the foetal body to get the head out of the hollow. This can be overcome in some cases by force, or under anaesthesia, but sometimes version, even under full anaesthesia, is impossible with safety. It has been the policy of the unit at St. David's Hospital not to attempt version under anaesthesia, so that the figures for persistent breech, previously quoted, are those for foetuses on which external version without anaesthesia had failed. Previously, at a time when the writer practised external version under anaesthesia, it was found that cases in which this failed had always a marked degree of uterine abnormality.

In 5 cases of the 10 presented in the breech series, the oblique lie of the foetus *in utero* was very obvious, with the head well impacted in one cornu of the uterus and the breech fixed in the pelvis. The foetal head in the maternal flank exhibited, as with vertex presenting cases, the flanking with overlie sign. Two of the five cases which exhibited this sign proved to have severe types of sub-septate uteri (Figs. 19 and 24) and another a uterus unicornus (Fig. 26).

Outcome of Breech Cases

Two breech cases in the series were delivered by lower uterine segment Caesarean section, one because the baby was thought to be large, and the other because of a type IV placenta praevia. There was one case of post-partum haemorrhage and one of retained placenta in the remainder. Like all breech deliveries at the hospital, the babies in the 8 cases which had a vaginal delivery were delivered by breech extraction under pentothal anaesthesia administered as soon as the buttocks were born.

In the case of the unicornual uterus, the cord prolapsed at full dilatation of the cervix, an event which precipitated the breech extraction. In the breech series 2 of the cases had foetal abnormalities incompatible with life. These were the only cases of foetal abnormality in the whole series.

Cystic Formation of the Uterus

The association of apparent cysts of the uterus with abnormalities of the organ is interesting. They appear to occur most commonly in either the early weeks or in the later weeks

of pregnancy. Their presence always denotes an advanced degree of uterine abnormality.

In the series 5 cases of "cystic" formation of the uterus were seen and 2 cases of Piscacek's sign. A sixth case of cystic formation occurred in one of the cases in the series in a subsequent pregnancy after completion of the investigation and this has been added (Case No. 6944, Table VI, Figs. 63 and 117). Of the cysts, 1 was seen in early pregnancy and 5 in late pregnancy. Two of the cases in late pregnancy failed to attend for hysterography, but all the facts in each case pointed towards a severe degree of uterine abnormality. One of the cases exhibiting Piscacek's sign also failed to attend. This patient developed a persistent breech presentation and was delivered as an extended breech at term. Exploration of the uterus after delivery revealed the customary bilateral cornual pocketing of the uterus.

The case histories and findings of the cases which were successfully followed up are as follows.

Case No. 4093 (Fig. 70)

Primigravida, aged 27. Previous operation for ectopic gestation. In the pregnancy under review, from the eighth to the tenth week, the patient suffered intermittent episodes of crampy abdominal pain accompanied by slight vaginal bleeding. When seen at 10 weeks the uterine size corresponded to that of a 10-weeks gestation. There was a protuberance in the outline of the left border of the uterus, with softening of this region as compared with the other side. The external cervical ostium was closed. There was no uterine or pelvic tenderness and no adnexal swellings were palpable. A threatened abortion of a pregnancy in a uterus exhibiting Piscacek's sign was diagnosed.

The patient was not seen again till the 32nd week when she was admitted in premature labour. After a labour lasting 13 hours the patient had an assisted delivery with Wrigley's forceps. The placenta was retained in a uterus exhibiting marked triangular spasm. Hysterography was carried out 10 weeks after delivery. The uterus at this stage was sub-involuted (Fig. 70).

Case No. 22838 (Fig. 71)

Primigravida, aged 25. Admitted to hospital as threatened abortion at 15 weeks. My note on the pelvic examination performed at this juncture reads, with diagrams drawn at the time, "soft cystic mass in pelvis towards left side the size of a fourteen weeks' pregnancy with accompanying harder mass on the right side. The right mass is smaller (about ten weeks) and seems more related to the cervix than the left mass. Probably pregnancy in a bicornuate uterus but query left ovarian cyst with pregnancy."

The patient was treated expectantly. There was no further bleeding or pain. For the rest of her pregnancy the patient remained symptomless and the gestation appeared to progress normally. When seen later at the 34th week signs of abnormality of the uterus did not appear to have been noted.

At 38 weeks the patient was admitted to hospital with toxaemia of pregnancy. At this stage there was noticeable asymmetry in the shape of the fundus of the uterus with fundal notching and a well marked "limb flanking with overlie" sign. Surgical induction was carried out at 39 weeks because of the toxaemia. The head was well down and the cervix "ripe" and effaced. Labour pains ensued shortly afterwards and the patient had a normal delivery after a labour lasting 7 hours. The placenta was expressed. During uterine contractions in labour the uterine horns were easily palpable. After delivery exploration of the uterus was carried out under pentothal anaesthesia and revealed marked bilateral cornual pocketing. No spasm effects were exhibited. There were no palpable abnormal swellings. Hysterography was carried out 16 weeks after delivery (Fig. 71).

Case No. 21577 (Fig. 19)

Primigravida, aged 25. The patient was first seen at the clinic at 39 weeks. The fundal height corresponded to a pregnancy of 36 weeks. The breech presented. There was a well-pronounced cystic swelling which appeared to be closely adherent to the left cornu of the uterus with the baby's head in the other cornu (Fig. Y).

Movement of the cyst caused only a slight corresponding movement of the uterus. The cyst could be "wandered" across the abdomen within certain limits, nevertheless it appeared to grow more tense when the uterus contracted. Owing to the unusual mobility of the cyst an uterine abnormality was not diagnosed with

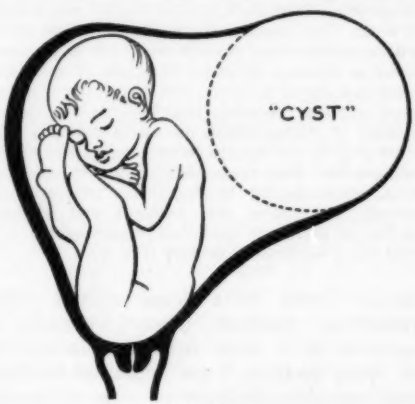


FIG. Y

complete confidence. The patient had an easy breech delivery at term by the extraction method already described, after a labour lasting 6 hours. The placenta was expressed. Whilst in labour there was no doubt about the origin of the cyst as it became very tense and fixed with each uterine contraction. Post-delivery exploration of the uterus showed marked bilateral pocketing without spasm. There was a depression at the fundus of the uterus deep enough to fit the space between the thumb and forefinger of the exploring hand.

The placenta site was palpated in the left cornu which was the site of the original uterine cyst. Hysterography was carried out 10 weeks after delivery (Fig. 19). (See also Addendum and Fig. 119.)

Case No. 21093 (*Fig. 72*)

Primigravida, aged 25. The patient was seen for the first time when she was admitted in labour at term. There was a cystic protuberance of the left cornu of the uterus. The vertex presented. The breech was palpable in the right cornu and the foetal limbs (presumably the legs) were ballotted inside the cyst between the pains. The cyst became tense during each uterine contraction. This cyst was not mobile like the previous one described and there was never any doubt about its origin.

Forceps delivery was carried out for delay in the second stage after a labour of 16 hours.

The uterus was explored after delivery and the placenta removed manually from a unilateral pocket at the left cornu of the uterus. The uterus exhibited spasm at the junction of upper and lower uterine segments.

Hysterography was carried out 11 months after delivery (Fig. 72).

Case No. 6944 (*Fig. 63*) (See also Table VI)

A known case of sub-septate uterus following hysterography taken after and because of a second abortion. The patient was seen at intervals throughout her pregnancy. The abnormal outline of the uterus was always demonstrable. "Limb flanking with overlie" was present at 36 weeks. Cystic swelling of the left cornu of the uterus was demonstrable from the 38th week. The patient was admitted in labour at 42 weeks. The cystic protuberance was still in evidence in labour, and though it was not so marked as those previously described, an opportunity was taken of photographing the uterus during a contraction (Fig. 117). A forceps delivery was carried out by an independent observer for delay in the second stage after a labour lasting 10 hours. The placenta was expressed. The uterus was explored and bilateral pocketing of the uterus confirmed. Hysterography was carried out 6 weeks after delivery (Fig. 63).

Baxter (1954), in a paper entitled "The asymmetrical pregnant uterus", presents a description of 4 cases. After examination of their X-ray pictures, I am impressed by their almost complete similarity to cases of uterine abnormality presenting as cysts of the uterus that I have seen and included above. Only one of Baxter's cases had a follow-up exploration and this "did not reveal any uterine abnormality". But even this diagnostic procedure can be misleading on occasions as is already illustrated in the text of this paper. His cases were not subjected to hysterography, otherwise I feel they might have been given a different classification.

Way (1945), in his first series, describes a pregnancy at 36 weeks which was thought to be complicated by an ovarian cyst, but at laparotomy the cyst proved to be the other horn of a "uterus bicornis-unicorpus-unicollis".

Falls (1928, 1939) reports a case in the early weeks which was diagnosed as an angular pregnancy, but which later proved to be a pregnancy in a bicornuate uterus. He draws attention to the manner in which the unilateral swelling of one horn of a bicornuate or arcuate uterus may simulate either an ovarian cyst or a fibroid in association with pregnancy.

FitzGerald (1952) reports a case of cystic swelling in the pelvis in association with a 12-weeks pregnancy. This could not be distinguished entirely from an ovarian cyst accompanying pregnancy and laparotomy was carried out. At operation the cystic swelling was so markedly one-sided in the uterus that an angular pregnancy was diagnosed. This diagnosis persisted until a Caesarean section was carried out at 42 weeks, because of foetal distress in a baby presenting by the breech. It was then realized that the condition had, in fact, been a normal pregnancy in a bicornuate uterus.

The sequence of events in this reported case is illustrative of that found with uterine abnormalities generally, viz., early cystic formation of the uterus, an irregular shaped uterus suggestive of angular pregnancy, persisting irregularity of uterine outline throughout pregnancy and finally a persistent breech presentation.

Early pregnancy in a malformed uterus often raises the possibility of angular pregnancy in the differential diagnosis, especially if the condition is associated with abdominal pain and vaginal bleeding, symptoms which are also not unusual in cases of pregnancy in malformed uteri. Munro Kerr and Moir (1949) present several examples of angular pregnancy and review the

literature on the subject. I am not entirely convinced after examination of this that the majority of cases presented as "angular pregnancy" are not, in fact, just further variations of presentation of pregnancy in a malformed uterus, or perhaps borderline interstitial pregnancies or a combination of both. For example, the picture which they present of Gibberd's case (p. 749) shows a very definite septum at the fundus of the uterus. If there is such an entity as "angular pregnancy" I feel it should fit in with DeLee and Greenhill's (1947) interpretation, which states simply that in true angular pregnancy the irregular outline of the uterus does not persist and there is a gradual return to normal symmetry after the early months. After all, implantation of the placenta in the cornu of the uterus is a frequent occurrence and is not confined entirely to cases of uterine abnormality. Nevertheless the finding of an irregular shaped uterus in the early weeks of pregnancy should make one think first of a possible uterine abnormality, and, even if correction takes place as pregnancy proceeds, as DeLee and Greenhill describe, one should still be suspicious and watch for the more confirmatory signs of the condition towards the end of pregnancy, especially with reference to foetal attitude. For it is my experience that these apparent, self-correcting malformations of early pregnancy can be heralds of an underlying uterine abnormality. The uterus exhibiting a positive Piscacek's sign probably represents a pregnancy in a uterus with a lesser degree of abnormality than one in which the pregnant horn takes on a cystic appearance.

Abortion

From Table VII which gives the incidence of various complications of pregnancy in the obstetric life of 23 parous patients with uterine abnormalities, we find that abortion ranks first with an occurrence rate of 24·5 per cent. This is in keeping with the findings of the following writers: Way (1947), 26 per cent; Miller (1922), 40 per cent; Findley (1926), 39·6 per cent; Taylor (1943), 25 per cent; Fenton and Singh (1952), for their series as a whole, 26 per cent, for their cases of sub-septate uteri, 37 per cent; Baker *et al.* (1953), 71 per cent in their series as a whole, 27 per cent in their cases of bicornuate uteri.

Munro Kerr and Moir (1949), quoting other authors, give the incidence of abortion in the country generally as about 20 per cent. They point out how difficult it is to compute the incidence of abortion, as the number of very early abortions and of criminal abortions cannot be determined. So at face value it appears that there is little difference between the abortion rate in cases of uterine abnormalities and in that of the country as a whole. But the figures for the country as a whole include cases derived from both malformed uteri and from criminally induced abortions, as well as the other accepted causes of abortion, so it is to be expected that the figure would be high. Thus for a more helpful comparison we should want to know the abortion rate as it refers to completely normal uteri.

The obstetric histories were analyzed of 43 patients who, on hysterography, had a completely normal picture. These patients had between them 86 pregnancies. There were 6 abortions in this small series, an incidence of 7 per cent. This compares with the findings of Baker *et al.* (1953) who give the abortion rate for normal uteri as 5·6 per cent.

Retained Placenta

In the series as a whole there were 20 cases of retained placenta. The 12 cases associated with hysterographically proved uterine abnormality have already been commented upon in the text. Of these 20 cases, 19 exhibited "triangular spasm". In the one case which did not exhibit spasm, the placenta was still adherent at the fundus in a normal uterus. The placental site was cornual in 13 cases and had not been defined in 5. In 11 of the 13 cases in which the placental site was cornual, the placenta was actually removed from the region of the cornu where it was partially held by the cornual spasm. In the other two cases the placenta was, in one, lying separated in the uterine cavity, in the other, partially held by the spasm at the junction of the upper and lower segments. Only one uterus of those investigated by hysterography, which had retained placentae and

exhibited triangular spasm proved to have a borderline picture (No. 23694, Fig. 97). The placental site in this case was on the posterior wall.

It appears, therefore, that abnormally shaped uteri are responsible for the large majority of cases of retained placenta. These are the uteri which tend to exhibit spasm characteristics at the three points of preference already described, viz., the cornual pocket openings and at the junction of the upper and lower segments, giving the syndrome of triangular spasm. There is no doubt that these spasm effects can be initiated by oxytocic drugs in combination with uterine manipulation as is suggested by the high incidence of retained placenta after the 12 cases of forceps delivery (Table V). That the tendency to spasm effects need not be recurrent is supported by the normal uterine outline exhibited by the two cases with a recurrent history of retained placenta (Table II).

Free Head at Term

The incidence of free head at term in primigravidae—9 per cent in the series as a whole (Table VIII), 15·6 per cent in the pre-diagnosed cases (Table X, A), represents an important finding in these cases. Occasionally the finding may be the only indication of a uterine abnormality. Certainly when a free head is found after the 37th week in a primigravida, after elimination of the other recognized causes for the head remaining free, I always look carefully for other accompanying signs of uterine abnormality.

The free head is probably due to the delayed formation of the lower segment which may not take place until labour is well advanced (Hunter, 1950).

Inco-ordinate Uterine Action

Six cases out of the 11 primigravidae in the series (Table V) who had a free head at term also exhibited inco-ordinate uterine action in labour and had labours lasting more than 24 hours. In 3 of them the labour lasted more than 40 hours. One was delivered after 42 hours by lower uterine segment Caesarean section and the other 2, after labours lasting 51 hours and 50 hours respectively, were delivered by forceps, full dilatation of the cervix having been attained by intravenous pethidine-pitocin drip infusion.

Four per cent of the cases in the pre-diagnosed series of primigravid patients exhibited inco-ordinate uterine action. This is not an unduly high figure and is probably in keeping with the incidence of the inco-ordinate uterine action in the hospital as a whole. The rise in incidence, however, to more than 50 per cent in cases which exhibited previously a free head at term is significant.

Postmature or Premature Deliveries

Falls (1939) also found a high incidence of postmature and premature deliveries in his cases.

Four cases in the present series went as far as 42 weeks and 3 cases to the 43rd week. Two cases in all had a surgical induction for "postmaturity". Four cases in the series came into labour before the 36th week of pregnancy.

It has already been stated previously in the text that a number of cases at the commencement of the investigation were X-rayed because they had premature deliveries. All of these had normal hysterographs.

Foetal Distress

Falls (1939) in his series lays great stress on the high incidence of foetal distress and irregularities of the foetal heart in labour. In this series only 3 cases of distress occurred to such an extent as to demand immediate delivery. Two were delivered by forceps, one in a parous patient and the other in a primigravida. The third case in a primigravida was treated by lower uterine segment Caesarean section.

Another 5 cases demonstrated episodes of foetal heart rate variations sufficient to suggest foetal distress at the time, but these either settled completely or did not advance sufficiently to warrant interference, and all cases ended in normal deliveries.

Sub-Involution

In 25 of the 65 cases with proved uterine abnormalities involution in the puerperium was

delayed in that the uterus was still palpable two inches above the symphysis pubis by the ninth day. This was not checked in every case by the writer, but I see no reason to doubt the accuracy of the findings.

Twin Pregnancies

Berkeley, Bonney and Macleod (1938) state that the incidence of twin pregnancy in cases of uterine abnormality is as high as 1 in 12 pregnancies, compared with the overall rate of 1 in 189 pregnancies.

There were 2 cases of twins in my series.

Toxaemia of Pregnancy

Hunter (1950) states that toxaemia of pregnancy is relatively frequent in cases of uterine abnormality. In my series there were 12 cases which were admitted to hospital with a blood pressure over 140/90 with or without other accompanying signs of toxaemia—an incidence of 18·4 per cent.

Foetal Size

The average weight of the babies on delivery was 7·4 pounds.

Maternal Morbidity

In spite of the unusual number of uterine explorations carried out in the investigation there was no increase in maternal morbidity over the other unexplored cases in the hospital.

Commentary

With the exception of the series by Falls (1928, 1939) and that of Way (1945, 1947) and this present series, no report of a large personal collection of cases of minor degrees of uterine abnormalities in relation to pregnancy has appeared in the literature. The literature is already replete with isolated reports of pregnancies in abnormal uteri of one type and another and with small collections of the more advanced types of lesion. Any large series of cases are either reviews of the literature, like that of Findley (1926), Jarcho (1946) and Baker *et al.* (1953) or are reviews of a single hospital's statistics, like those of Smith (1931) and Fenton and Singh (1952). The cases too have been collected over a long period of years —31 years in the case of Smith. Even Falls's collection has been over an extended period of 13 years. Way's second series (1947) of 19 cases was collected during a period of one year. My collection has been over a period of 18 months, so that the only previous report with which this collection of cases compares is that of Way. It is felt that these short-term reviews are more valuable in presenting a truer picture of the incidence and significance of uterine abnormality in relation to pregnancy.

As this series of cases deals with the more minor degrees of abnormality of the uterine body, no attempt has been made in the cases to ascertain if any associated lesion of the renal tract also existed. In only one case in the investigation was an associated lesion of the vagina encountered. This took the form of a septum lying close against one wall of the vagina and only came to light because the patient suffered a severe tear of the vaginal integument and perineal body during a normal delivery. This was one of the cases which did not report back for hysterography.

There appears to be much confusion in the literature concerning the classification of the various types of uterine abnormality and each successive writer, attempting to simplify the situation, has only added more confusion to the issue. This is one reason why I have purposely avoided the newer terminology of writers like Way (1945) and Hunter (1950), as I found that X-ray investigations of my own cases have made them fit more accurately the patterns as described by earlier writers; and above all, I have found the classification of Jarcho (1946) the most useful and descriptive, and, at the same time, remaining the most simple.

Falls (1939), describing 155 cases of pregnancy in the "arcuate uterus", defines arcuate uterus as that form of bicornuate uterus in which the normal fusion of the two horns in embryonic life stopped just short of completion, forming an organ which, in the non-pregnant state, can with difficulty be differentiated from a normal uterus but which, when pregnant, exhibits marked irregularities of contour. He

goes on to say "The most extreme grades of bicornuate uterus are for the most part anatomical curiosities, which rarely have clinical significance. If such uteri contain a pregnancy they usually abort the product of conception or carry it through and present an indication for Caesarean section at term because of malposition or dystocia or both." He does not appear to recognize any of the other forms of the minor degrees of uterine abnormalities as being responsible for his unusual antenatal findings. He gives certain diagnostic criteria for recognizing the arcuate uterus. These are axial deviation of the foetus, broadening of the fundus, dimpling of the fundus and free head at term. Subsequent writers, basing their criteria of diagnosis on Falls's teaching, appear to follow the line of Fenton and Singh (1952) and state that the diagnostic signs of septate and sub-septate uterus are likely to be obscure. Jarcho (1946) too says that, if the uterus exhibits signs of irregularity, then the diagnosis is likely to be one of arcuate uterus.

Way (1945) on the other hand, sets the ball rolling in the opposite direction and refuses to recognize arcuate uterus as the entity described by Jarcho. He describes it as a uterus having a visible dimple exteriorly, but having a normal interior contour. He presents 5 such cases in which the external deformity was either "felt quite clearly", or was "seen at Caesarean section", but the cavity was normal. This, he says, was confirmed radiologically, but he does not define his X-ray expression of a normal uterine cavity. The arcuate uterus, according to Way, does not deviate from the normal in pregnancy.

Hunter (1950) supports Way in his description of arcuate uterus, but confuses matters by adding to his classification "uterus cordiformis", which has already been described by Jarcho as synonymous with uterus arcuatus.

I cannot agree with Falls and Jarcho that arcuate uterus is a separate entity in that it differs in behaviour or in its revealed diagnostic signs from uterus sub-septus or uterus bicornis. Nor can I agree with Way in that the interior of the uterus is normal. I do, however, agree with Jarcho's anatomical description of the entity.

Way also subdivides uterus bicornis into "uterus bicornis-unicorpus-unicollis" and "uterus bicornis-bicorpus-unicollis" depending on whether the dividing septum does or does not extend as far as the internal os. He states that this distinction should be made as there is a difference in behaviour in the two types. In the present series this distinction cannot be made. The X-ray pictures (Figs. 42, 64 and 71) are, in my opinion, those of bicornuate uteri which in Way's classification should be uterus bicornis-bicorpus-unicollis, but technically the septum does not reach as far as the internal os in any of them. These cases differed little in their behaviour from the other cases presented in the series. It is interesting to note the unusual length of the supra-vaginal cervical canal in these cases of advanced uterine abnormality.

Way in his series presents 5 cases of subseptate uterus and 31 cases of "uterus bicornis-unicorpus-unicollis". These latter in this present series would probably be classified as severe subseptate or, perhaps, sub-septate. He presents no cases of bicornuate uterus or what in his classification would be "uterus bicornis-bicorpus-unicollis". This proportion of uterus sub-septate to uterus bicornis-unicorpus-unicollis appears to be out of tune considering the frequency with which, in the present series, the more minor types of abnormality were detected. From close examination of the histories of his cases (as he presents them), Way appears to have employed the following criteria in diagnosis:

(1) On exploration the palpation of a "septum" with no palpable uterine irregularity was diagnosed as sub-septate.

(2) The finding of uterine irregularity before delivery accompanied on exploration by a "septum" or "bulge" was diagnosed as uterus bicornis-unicorpus-unicollis.

(3) Visualization of the exterior surface of the uterus at laparotomy or Caesarean section:
   (*a*) if depression exteriorly with "septum" or "bulge" in cavity it was diagnosed uterus bicornis-unicorpus-unicollis.
   (*b*) if smooth surface exteriorly and "septum" interiorly it was diagnosed subseptate.

Way palpated a "septum" on 9 occasions in the 18 cases presented in his first paper. Each was apparently a very marked anatomical structure. On occasion he describes it as "two inches long". Five of these cases he diagnosed as sub-septate, but, as the other 4 were accompanied by abnormal uterine shapes, he diagnosed them as uterus bicornis-unicorpus-unicollis. In no case in this series can I say that I felt a "septum" which in any way could be regarded as approaching the anatomical structure described by Way. What I felt as a septum has been a depression in the fundal wall of the uterus which demarked dramatically, like a water-shed, the approaches to the bilateral pocketing effect at the uterine cornua. The most common finding in this series was the bilateral pocketing effect without septum formation. When I did palpate a "septum" or dividing line it was found later, on hysterography, that the abnormality of the uterus was of an advanced nature, either a severe sub-septate or a bicornuate configuration. But occasionally even the palpation of a septum was misleading and I was surprised on seeing the X-ray picture to find that the degree of abnormality was not so advanced as I had diagnosed clinically. Occasionally also the reverse was the case.

It is interesting to note that Way, in his second paper, when he presents 22 cases of uterus bicornis-unicorpus-unicollis, does not describe the presence of a "septum" in any of them.

Therefore I cannot type any of my cases by Way's criteria as sub-septate, as I did not feel a "septum", but my findings of bilateral pocketing, in conjunction with the X-ray findings, induce me to make my own classification of sub-septate uterus. This conforms closely with Jarcho's description of sub-septate uterus. True, some of these cases may technically have been cases of arcuate uterus, but one cannot make such a diagnosis without inspecting the peritoneal surface of the uterus—palpation is not enough. Apropos of this, I have always been impressed by the complete lack of correlation between the exterior appearance of the uteri examined and their internal contour behaviour, as found just after parturition. Many uteri with marked bilateral pocketing and even septum formation interiorly showed no evidence exteriorly of what lay beneath. Therefore, I think it is unsafe to rely on any method other than hysterography to make a classification of clinically diagnosed cases of uterine abnormality. I have accordingly typed my cases purely in accordance with their hysterographic pictures and, as stated, this is done realizing that perhaps many of my sub-septate uteri are truly arcuate.

There appears to be a great hesitancy on the part of Way to suspect that any of his cases may have been examples of uterus bicornis-bicorpus-unicollis. This is in keeping with the teaching in the literature, which always associates bicornuate uteri with a very bad prognosis for pregnancy. Way's incidence for uterus bicornis-bicorpus-unicollis is 3 cases in 1,800 admissions to the maternity department and 10,000 to the gynaecology department. Jarcho also paints a gloomy picture. He states that pregnancy can occur in either or both horns and stresses the dangers to both mother and foetus from abortion, incarceration of the non-pregnant horn, etc. The impression gained from the literature is that the septum must always remain a definite entity throughout pregnancy to divide the uterus into two distinct cavities, the non-pregnant one giving rise to a high complication rate. This is probably true in the types where the septum persists and in the early weeks of pregnancy, but I think the incidence of complication is not so high as we have been led to believe in the past. In cases seen in the series, the septum appeared to be more or less taken up into the fundal muscle tissue in association with the growing uterus and the two cavities became one with only the bizarre exterior shapes or unusual foetal attitude to give an indication of the true state of affairs.

Summary

(1) Sixty-five cases of minor degrees of uterine abnormalities in association with pregnancy found in an 18-months investigation period are presented with their hysterograms and reviewed. Another 28 probable and a further 107 possible cases are referred to in the text. The incidence of the condition is thought to be in the neighbourhood of 10 per cent.

(2) New criteria for the diagnosis of the condition are presented and these with the old criteria are assessed.

(3) A standard of normality of uterine outline for the human uterus is defined.

(4) It is advocated that the classification of abnormalities should be made on hysterography as other methods, based on palpation of the uterus and visualization of the uterine surface, can be misleading.

(5) The dangers of the condition to mother and baby have been over-emphasized in the past, as the majority of cases go through pregnancy and labour quite normally.

(6) The complications of pregnancy in association with the condition are abortion, breech presentation, retained placenta, sub-involution and inco-ordinate uterine action (when the case is associated with a free head at term in primigravidae).

(7) Evidence is presented to suggest that uterine abnormalities in association with extended legs are the primary cause of breech presentation.

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Addendum

Since this paper was completed for publication two of the severe cases of uterine abnormality, already reported in the text, were subjected to lower uterine segment Caesarean section in subsequent pregnancies. The surface of the uterus in each case was photographed after delivery of the baby.

Case No. 21577 (Fig. 19). Breech delivery as a primigravida—see Cystic Uterus. Shoulder presentation—prolapse of cord in early labour at term (Fig. 119).

Case No. 21660 (Fig. 42 and Table VI). Extended breech presentation at term—elective operation (Fig. 120).

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ERGOT AND THE NON-PREGNANT UTERUS

BY

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THE efficacy of ergot in arresting haemorrhage after delivery is undoubted and, by analogy, ergot has been thought to hold a place in the treatment of haemorrhage in gynaecological disease. For years Martindale's *Extra Pharmacopoeia* supported two conflicting views when it described ergometrine as a palliative measure in menorrhagia, and crude ergot as an emmenagogue (Martindale, 1941). Thirty years ago Howard Kelly was in no doubt when he wrote of the treatment of menorrhagia, "Ergot, ingested in the past by thousands of tons, is useless" (Kelly, 1928). Today the *British Obstetric and Gynaecological Practice* recommends ergot in acute episodes of serious haemorrhage from metropathia but adds that this use is traditional rather than efficacious (Jeffcoate, 1955).

The present paper reports a study of the effects of a crude ergot preparation and two ergot alkaloids on the contractility of the intact non-pregnant uterus. This is not straightforward like similar studies on the pregnant and puerperal uterus as the type of spontaneous activity in non-pregnant uteri varies with the phase of the menstrual cycle. In the first half of the cycle the characteristic pattern is one of rapid, feeble contractions or A waves, whereas later in the cycle (or during menstruation after ovulation) slower and many times more powerful contractions, or B waves, are the dominant feature (Moir, 1944). The several ergot preparations have been tried at all stages of the menstrual cycle and in a few anovulatory cycles.

METHOD

Records of uterine activity were obtained from 33 volunteer patients by the intra-uterine balloon method (Moir, 1934). Only cases giving a normal menstrual history were included in the series. Where curettage was indicated on medical grounds, endometrial biopsy was obtained to give more objective information concerning the endocrine conditions prevailing at the time of the study.

With the usual antiseptic precautions the cervix was exposed and a small, collapsed, sterile balloon mounted on a hollow uterine sound was passed into the cavity of the uterus under direct vision and without anaesthesia. When in place the balloon was filled with water to 15 mm. of mercury initial distending pressure. As the maximum capacity of the balloon was designed not to exceed 2 ml., this initial distending pressure was "balanced" by the elasticity of the balloon walls. The balloon was then connected by water-filled pressure-tubing to a very fine tambour or, in appropriate cases, to a mercury manometer recording on smoked paper.

After a suitable control period of recording, the ergot preparation was given and the effect noted.

RESULTS

Ergotamine

In the first half of the menstrual cycle when A waves formed the characteristic pattern of spontaneous uterine activity, ergotamine had little effect by intramuscular injection. A slight increase in the amplitude of the A waves, with

some delayed rise in tone, was the only response (Fig. 1a). In the second half of the cycle, when the larger B waves were present, a similar slow rise in tone occurred after 25 minutes in 2 cases. Uterine activity seemed less regular and the records as a whole bore only slight resemblance to similar studies in the puerperal uterus (Moir, 1932) (Fig. 1b).

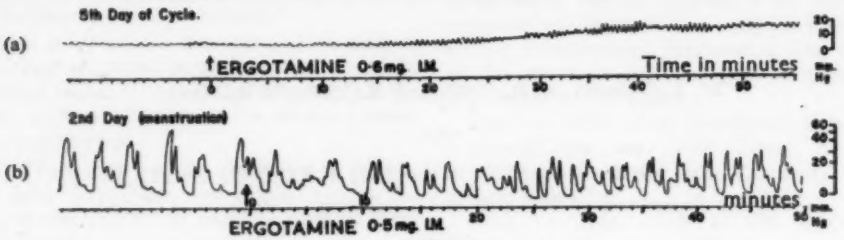

FIG. 1

The effect of ergotamine tartrate on the non-pregnant uterus.

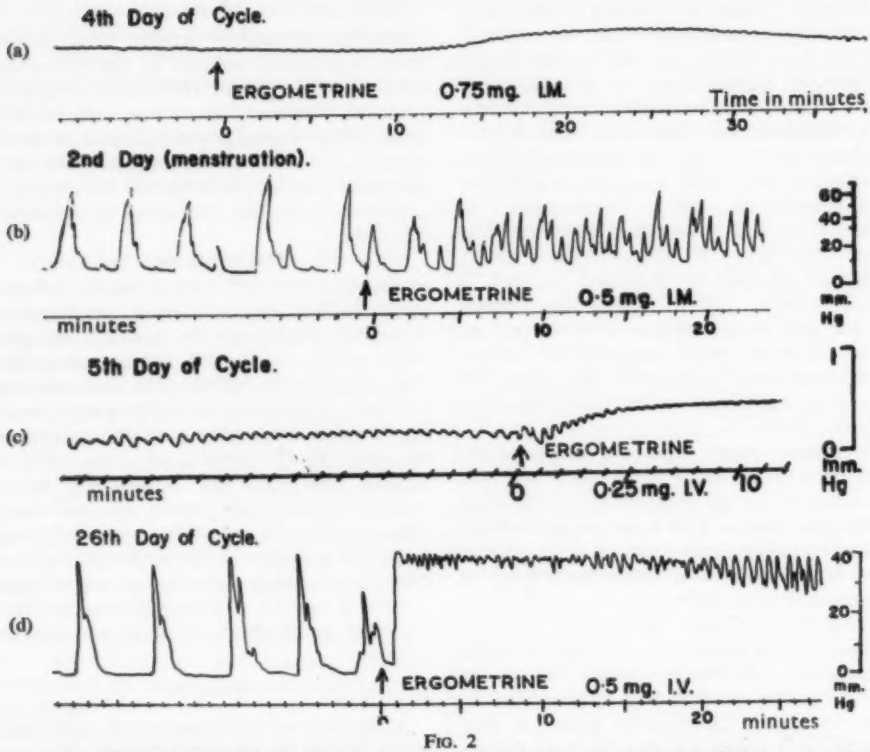

FIG. 2

The effect of ergometrine on the non-pregnant uterus (a and c). In the first half of the menstrual cycle, when the rapid, feeble A waves form the characteristic pattern of uterine activity, ergometrine produces a very slight rise in tone (b and d). In the presence of the slow, strong B waves of menstruation and the pre-menstrual week, ergometrine induces a typical oxytocic response.

Ergometrine

When the rapid, feeble A waves were being recorded in the first half of the cycle, a slow rise in tone with or without an increase in amplitude was the response to ergometrine by intramuscular injection (Fig. 2a). A more definite picture, superficially resembling an oxytocic response, was seen when ergometrine was given intravenously. In some cases the rise in tone was slow. In others, a steep rise in base-line was recorded but, as this did not amount to more than a few millimetres of mercury (Fig. 2c), it was not strictly an oxytocic response as originally described (Dudley and Moir, 1935).

In the second half of the cycle, when the slow, strong B waves were the characteristic pattern, a mild oxytocic effect followed the intramuscular injection of ergometrine after 7 to 13 minutes (Fig. 2b). By intravenous injection ergometrine elicited the "classical" oxytocic response with a rise in tone of up to 35 mm. of mercury above the resting level (Fig. 2d). The frequency of contractions was considerably augmented while the amplitude was diminished. A temporary spasm had been induced.

Liquid Extract of Ergot, B.P.1932

Beyond a slight increase in tone, oral administration of liquid extract of ergot had no significant effect on uterine motility in the non-pregnant uterus (Fig. 3a, b).

Anovulatory Cycles

In anovulatory cycles where A waves formed the characteristic pattern no significant oxytocic effect was elicited by ergometrine. A slight rise in tone was the only response (Fig. 3c). Details of all the investigations are given in Table I.

Discussion and Conclusions

The general conclusion from these studies is that ergot preparations do have an effect on the non-pregnant uterus, the response differing only in time and magnitude with the choice of the alkaloid and its route of administration. In the

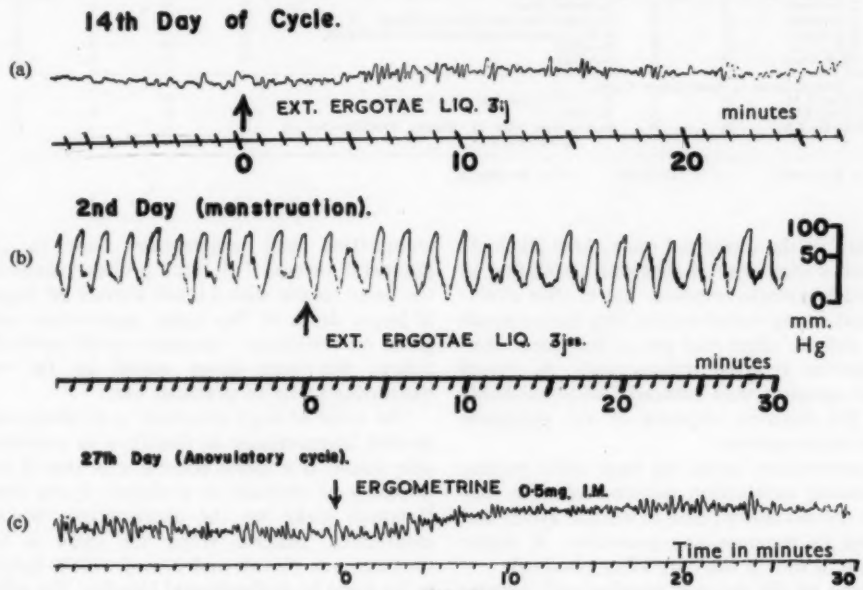

Fig. 3

(a and b) Liquid extract of ergot has little effect on uterine motility. (c) In an anovulatory cycle ergometrine produces a minor increase in uterine tone.

TABLE I

Case No.	Dose	Day of Menstrual Cycle	Type of Uterine Activity (waves)	Result	Details of Uterine Response			Duration of Tracing After Drug (minutes)
					Frequency	Amplitude	Tone	
	ERGOTAMINE:							
1	0·5 mg. I.M.	5	A	No definite effect	0	0	0	45
2	0·6 mg. I.M.	5	A	Increased amplitude with slow rise in base-line after 25 minutes	0	+	+	58
3	0·5 mg. I.M.	10	A	No definite effect	0	0	0	56
4	0·5 mg. I.M.	14	A	Slight increase in amplitude	−	+	0	43
5	0·5 mg. I.M.	16	A	No effect	0	0	0	45
6	0·5 mg. I.M.	17	A	Increased tone after 8 minutes	−	+	+	45
7	0·5 mg. I.M.	17	Early B	Rise in base-line after 25 minutes	+	0	0	35
8	0·5 mg. I.M.	20	B	Rise in base-line after 25 minutes	+	0	+	45
9	0·5 mg. I.M.	1	B	No definite effect	+			34
10	0·5 mg. I.M.	2	B	Irregular activity, especially after 25 minutes	+	−	0	50
	ERGOMETRINE (by intramuscular injection):							
11	0·75 mg. I.M.	4	A	Slow rise in base-line after 15 minutes	0	0	+	42
12	0·5 mg. I.M.	10	A	Slow rise in base-line after 6 minutes	0	+	+	17
13	0·5 mg. I.M.	20	B	Irregular activity after 13 minutes	0	−	+	31
14	0·5 mg. I.M.	24	B	Irregular activity after 12 minutes	+	−	+	26
15	0·5 mg. I.M.	2	B	Mild oxytocic effect after 7 minutes	+	−	+	24
	ERGOMETRINE (by intravenous injection):							
16	0·25 mg. I.V.	4	A	Oxytocic effect in 2 minutes	+	−	+	15
17	0·25 mg. I.V.	5	A	Slight rise in base-line after 1½ minutes	0	−	+	12
18	0·25 mg. I.V.	12	A	Oxytocic effect in 2 minutes	+	−	+	15
19	0·25 mg. I.V.	14	A	Slow rise in base-line after 1 minute	−	0	+	21
20	0·5 mg. I.V.	19	B	Oxytocic effect in 1 minute	+	−	+	44
21	0·5 mg. I.V.	20	B	Classical oxytocic effect in 1 minute	+	−	+	13
22	0·25 mg. I.V.	23	B	Oxytocic effect in 1 minute	+	−	+	20
23	0·5 mg. I.V.	26	B	Classical oxytocic effect in 1 minute	+		+	45
24	0·5 mg. I.V.	26	B	Classical oxytocic effect in 1 minute	+	−	+	27
25	0·25 mg. I.V	27	B	Classical oxytocic effect in 1 minute	+	−	+	30
	EXTRACTUM ERGOTAE LIQUIDUM (B.P.1932):							
26	2 drachms	5	A	Doubtful effect	0	0	+	24
27	2 drachms	14	A	Increased amplitude after 6 minutes	0	+	+	27
28	2 drachms	15	A	Slight increase in amplitude after 8 minutes	0	+	+	21
29	2 drachms	26	B	No effect	0	0	0	25
30	1½ drachms	2	B	No effect	0	0	0	30
	ERGOMETRINE in Anovulatory Cycles:							
31	0·5 mg. I.M.	27	A	Slow rise in base-line after 5 minutes	0	0	+	30
32	0·2 mg. I.V.	24	A	No effect	0	0	0	12
33	0·25 mg. I.V.	26	A	Raised tone after 11 minutes. Probably not an oxytocic effect	+	+	+	33

+ = Increased. − = Decreased. 0 = No change.

first half of the menstrual cycle these alkaloids produce a slight rise in tone not amounting to an actual oxytocic response. Later, after ovulation and during menstruation, they have a much more definite effect and this is best seen when ergometrine is given intravenously. A typical uterine spasm is then induced indistinguishable from the oxytocic response of the puerperal uterus to ergometrine.

In anovulatory cycles no such effect occurs. The resting contraction pattern resembles that of the pre-ovulatory phase of normal cycles and so does its response to ergometrine. A minor increase in tone is the only effect obtained.

Taking all the tracings together and judging from earlier studies, it seems that the non-pregnant uterus is much less sensitive to ergometrine and ergotamine than is the puerperal uterus. This fact probably explains the poor results with Liquid Extract of Ergot. If larger doses of this older preparation were given an "oxytocic" response would probably follow, but such doses would be far too nauseating to be of practical use.

The value of ergot alkaloids in dysfunctional uterine haemorrhage is therefore in considerable doubt. If a useful effect is ever seen it will probably be confined to ovulatory cycles when B waves make up the characteristic uterine contraction pattern. When the cycle is anovulatory, as Novak and Novak (1952) believe to be usual in dysfunctional bleeding, the effect of ergot is insignificant, a paltry rise in tone being the only response.

Apart from these considerations, it is still doubtful whether ergot alkaloids would have the same effect on both menorrhagia and post-partum haemorrhage as the source of the haemorrhage is different in the two cases. In menorrhagia, bleeding comes from the basal vessels of the endometrium. These vessels are superficial and are not subject to the haemostatic stranglehold that the myometrium exerts on maternal sinuses left open at the placental site. It is unlikely therefore that ergot alkaloids would quell the flow of menorrhagia in a way comparable to their control of post-partum haemorrhage.

Summary

(1) The effect of ergot preparations on the intact non-pregnant uterus has been recorded mechanically in 33 cases.

(2) In the first half of the menstrual cycle and during anovulatory cycles the only response is a slight increase in uterine tone.

(3) In the second half of normal cycles and during menstruation after ovulation, ergometrine induces an "oxytocic" effect.

(4) There is little evidence to support the use of ergot preparations in the control of haemorrhage from the non-pregnant uterus.

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PROTECTION BY PREGNANCY AGAINST THE DEVELOPMENT OF "INFARCTOID CARDIOPATHY" AND NEPHROCALCINOSIS

BY

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NUMEROUS earlier publications have dealt with the possible influence of pregnancy and of sex hormones upon the development of clinical or experimental cardiovascular diseases, but the relevant data are rather difficult to interpret (Selye, 1950; Stamler, Katz and Pick, 1954; Selye, Heuser and Horava, 1951–1955/56). More recent experiments on rats showed, however, that dihydrotachysterol, which produces severe arteriosclerosis of the Mönckeberg type in non-pregnant rats, is well tolerated during pregnancy (Selye, 1957).

During the past year, it has been demonstrated that certain corticoids (especially the highly potent 9-halogenated compounds) can so condition the cardiac muscle of rats that the oral administration of an excess of sodium phosphate regularly produces infarct-like, massive necroses in the myocardium. This is usually, but not always, associated with nephrocalcinosis (Selye and Renaud, 1957; Selye, 1958a). The entire literature concerning this "infarctoid cardiopathy", including its possible relationship to the spontaneous cardiac infarcts of man, has been surveyed elsewhere (Selye, 1958b).

The object of this communication is to report upon experiments which demonstrate that pregnancy offers a definite protection against the infarct-like phosphate-steroid-cardiopathy and the accompanying nephrocalcinosis. This finding is reminiscent of the inhibitory effect that gestation exerts upon the arteriosclerosis normally induced by dihydrotachysterol.

METHOD

Our experiments were performed on two groups, each consisting of 10 adult, female rats of the Sprague-Dawley strain, with an average initial body-weight of $315 \pm 3 \cdot 3$ g. and $228 \pm 3 \cdot 8$ g. respectively. The controls exhibited normal sexual cycles, while the experimental animals were 14- to 15-days pregnant at the beginning of the experiment.

Both groups were treated with 400 mg. of monosodium phosphate ($NaH_2PO_4 \cdot H_2O$) in 4 ml. of water, twice daily, by stomach tube. In addition, they received 250 μg. of 2α-methyl-9α-chlorocortisol (Me-Cl-COL), in the form of microcrystals of its acetate suspended in 0·2 ml. of water, once daily, subcutaneously. This combined phosphate-steroid treatment had previously been shown to be highly efficacious in eliciting the infarctoid cardiopathy.

Throughout the experiment, the rats of both groups were kept exclusively on the laboratory food, "Purina Fox Chow" of the Ralston Purina Company, and tap water.

The hearts and kidneys of all the animals which either died spontaneously or were killed at the end of the experiment were fixed in neutral formalin, for subsequent embedding in paraffin and staining with haematoxylin-phloxine (for the appraisal of general structure) as well as with von Kossa's silver nitrate technique (for the histochemical demonstration of calcium). The severity of the cardiac necroses and of the nephrocalcinosis was gauged in terms of an arbitrary scale of 0 to 3.

FIG. 1

Macroscopic appearance of the outer surface of the heart (top) and the cut surface of the kidney in a non-pregnant (left) and a pregnant animal, both of which received the same dose of Me-Cl-COL and NaH_2PO_4. The light patches of "infarctoid cardiopathy" and the concentric lines of nephrocalcinosis, that developed under the influence of this treatment in the non-pregnant control, are absent in the pregnant animal.

FIG. 2

Cut surface of the hearts shown in Figure 1. The miliary, infarct-like, white, necrotic patches in the non-pregnant animal (top) are distributed throughout both ventricles and are particularly conspicuous near the apex of the heart. No such lesions are observable in the interior of the pregnant animal's heart.

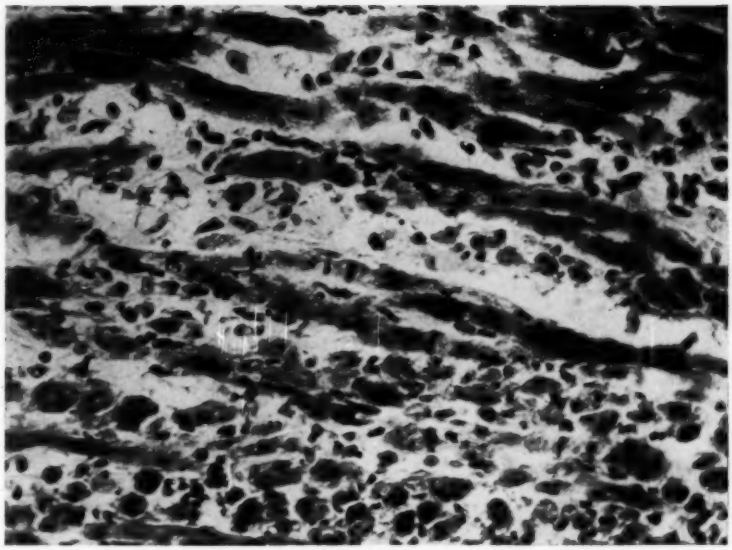

FIG. 3

Histological aspect of a necrotic patch in the heart of the non-pregnant animal shown in Figure 1. The muscle fibres throughout this field are in various stages of disintegration and the focus is invaded by histiocytes and polymorphonuclear leukocytes. Haematoxylin-phloxine. × 350.

Results

Between the third and fourth day of treatment, all the non-pregnant controls began to lose weight. Their fur became shaggy and they exhibited manifest clinical signs of cardiac insufficiency, such as cyanosis and dyspnoea. Five of these rats died between the third and sixth day of treatment, while the sixth had to be killed on the eighth day, because it was manifestly moribund.

Autopsy of these control animals revealed the characteristic, large, yellowish patches of myocardial necrosis, and intense nephrocalcinosis (Figs. 1 and 2). Histological study of the tissues showed that the myocardial lesions consist of necrotic patches, within which the muscle fibres first disintegrate, and are then invaded and replaced by histiocytes, polymorphonuclear cells and, eventually, a connective tissue scar (Fig. 3). In the kidney, numerous calcified cylinders were detectable, especially at the cortico-medullary junction line (Fig. 2).

In contrast, all of the pregnant rats remained perfectly healthy and their pregnancy continued without complication.

On the sixth day, when 50 per cent of the controls had died, the treatment of the surviving pregnant animals was discontinued; they all delivered healthy young, at approximately the normal time.

After delivery, the animals were killed, and histological study of their organs revealed no sign of phosphate-steroid-cardiopathy in the mothers or in their young. Also, there was no nephrocalcinosis in the newborn, although one of the mothers showed traces of renal calcification.

Discussion

It is evident, from these observations, that pregnancy can very effectively protect the rat against the development of the infarct-like cardiac lesions and the nephrocalcinosis that normally occur under the influence of combined treatment with Me-Cl-COL plus sodium phosphate. It remains to be seen whether the factor responsible for this protection against the infarctoid cardiopathy is the same as that which, in pregnant animals, prevents the development of arteriosclerosis after dihydrotachysterol treatment. Experiments are now under way to determine whether the protection against the infarctoid cardiopathy is due to the embryo, the placenta, or some (possibly hormonal) change in the maternal organism. The possibility must be considered that this kind of protection may be related in some way to the relatively low incidence of spontaneous infarcts in women.

Summary

Experiments on rats indicate that pregnancy offers considerable protection against the infarct-like cardiac necroses and the nephrocalcinosis that are normally produced by combined treatment with NaH_2PO_4 and certain corticoids such as 2α-methyl-9α-chlorocortisol (Me-Cl-COL).

The possible clinical implications of this finding are discussed.

Acknowledgments

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The author also wishes to acknowledge generous supplies of 2α-methyl-9α-chlorocortisol (Me-Cl-COL) from The Upjohn Company.

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POPULATION STRUCTURE AND THE APPARENT INCIDENCE OF CANCER—A STUDY OF ENDOMETRIAL CARCINOMA IN ENGLAND AND SOUTH INDIA

BY

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THE average age of incidence of a particular disease is rightly regarded as one of its important features. For cancers at various sites this point is used in the differential diagnosis when probabilities are considered. Thus innumerable students throughout the world have been taught that for a patient with irregular vaginal bleeding carcinoma of the body of the uterus is more likely than that of the cervix in older women, especially if nulliparous and post-menopausal. Indeed more accurate rules have been laid down as the result of careful statistical study of large series of cases, as well as those based on more general impressions. It must be emphasized, however, that these rules apply only for the particular conditions under which they were promulgated. Thus in hospital practice in England endometrial carcinoma and cervical are approximately equal in incidence (Towers, 1954). Rules laid down for England are, however, of little use in India where carcinoma of the body of the uterus is very much less frequent than that of the cervix. Endometrial cancer is regarded here as quite a rare disease and reports of single cases are considered worthy of publication in technical journals. No figures for an exact comparison appear to be available, those for this Institute being misleading because, being the main gynaecological centre equipped with radium in the State of Madras, we are sent an inordinate number of cancers of the cervix.

The position is complicated further by the different age-structures of the two populations. In a recent report (Rewell, 1957) an analysis of cervical cancer cases seen here over the past few years was presented and the age incidence found to be about 10 years younger than in England. Some reasons for this were suggested and discussed. It was, however, made clear that this lowered age-incidence was after due allowance had been made for the difference in the age-structures of the populations. In India there are many less people relatively in the older age-groups than is the case in England, so that in any disease of adults fewer cases would fall among older people in India and the average age of incidence would thus be lower than in England. This would be most marked for a disease more common among older people round about the age of 55 or over and less marked when the maximum incidence is among the younger, say round about 25.

This is made clear in Table I. The figures for the State of Madras are taken from the relevant volume of the census of India for 1951 (Venkateswaran, 1954). Those for England and Wales in 1954 are from the Registrar General's Report (1955). These are the latest figures available and were used in my previous report mentioned above where it was conceded that the two sets were not for the same period of time, but the Indian figures were not likely to have altered significantly in the 3-year interval between them. The female populations for successive 5-year age-groups between 20 and 64 have been expressed as percentages of the total between the two ages in the respective countries. It is seen that after the 40–44 age group the

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TABLE I

Ages	Percentage of Women 20–64		No. of Endometrial Cancers		"Corrected" No. for Madras
	England	Madras	Liverpool	Madras	
20–24	10·38	16·93	0	1	0·75
25–29	11·10	16·30	0	1	0·75
30–34	12·83	14·56	0	0	0
35–39	10·60	11·88	2	5	5
40–44	12·34	12·19	2	6	9
45–49	12·17	08·86	8	3	4·5
50–54	11·36	08·00	18	6	9
55–59	10·18	04·99	23	6	16
60–64	09·30	05·67	18	0	0
65–69			11	1	
70–74			4	0	
75–79			4	0	

proportion of the population at risk falls more sharply in Madras than in England. Five-year groups are few enough for ease of computation, yet small enough to demonstrate the effects discussed. It is, of course, well recognized that diseases of advancing years, such as cancers, are more common in ageing populations, but the effect of the ageing on the age incidence of individual diseases is often overlooked. The effects observed are made more clear if the English population is taken as the norm and the Madras figures adjusted on this basis than if the Indian population is taken as a basis. This is again purely a matter of convenience.

Now the Women's Hospital, Liverpool, and the Institute of Obstetrics and Gynaecology, Madras, treat about the same number of gynaecological in-patients each year, apart from the large number of women treated by radiotherapy in Madras. Dr. H. R. Harris of Liverpool has sent me the figures for endometrial cancer from there for the three and a half years from mid-1952 until the end of 1955. There were 92 cases, of which the age of two has not been recorded, but the mean age of the remainder is 57·8 years. In Madras over the same length of time, starting at the beginning of 1954, there were only 29 cases, the mean age being 45·1 years. The difference between these means is large and undoubtedly statistically significant and would appear at first sight to justify the statement that I have heard so often from doctors in India: "Cancers here all occur ten years younger than in the West." The difficulties of ascertaining the age of South Indian women have been discussed in my previous paper mentioned above and the results are obviously less useful for the present small series than for the much larger number of cervical cancers. However, they are all that is available and there is no reason to suppose that there is any factor which would direct the errors in any one direction rather than in another.

The peak of incidence of endometrial carcinoma thus falls in the 55–59 age group in England and in the Madrasi cases no such obvious peak appears when they are arranged in this way (Table I). However, the picture is altered if the Madras figures are "corrected" for the difference in the proportion of the population at risk falling into each of the age groups as compared with the proportion in England. This is done by multiplying the number of Madras cases in each age-group by the percentage of Madrasi women in the same group and dividing by the English percentage. The most striking effect of this manipulation is the threefold multiplication of the number of cases in the 55–59 age group which makes this the peak for Madras as well as for England.

The smallness of the original series from Madras makes it unwise to attempt to draw

other conclusions from this comparison, especially as there were no cases in some of the age-groups. It is, however, possible that the incidence of the disease is more spread out as regards age in Madras and less concentrated in the sixth and seventh decades. No conclusions can be drawn as to aetiology either, only two patients being recorded as diabetic and two as nulliparous. Unfortunately several were demonstrated only in curettings, the patients refusing further operation. One was a carcinoma *in situ*, no further malignant tissue being found in the panhysterectomy specimen. The disease in Madras was found not to differ from what is seen in England in any clinical or pathological feature.

Summary and Conclusions

Figures for the age incidence of carcinoma of the endometrium are presented from two centres, one in England and the other in South India. The disease is much less frequent in India than in England, but more frequent in younger women in India. However, allowance for the smaller proportion of older women in the Indian population shows that this difference is less real than appears at first sight. The series are too small for further conclusions to be drawn from them.

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ACUTE ADRENAL NECROSIS AND PREGNANCY

BY

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THIS report is mainly concerned with the clinical history of a patient who sustained an acute adrenal insufficiency at delivery. She survived the acute phase and gradually achieved full clinical recovery ten months from the onset.

CASE NOTES

Mrs. A.S., a primigravida, aged 25 years, living in the West of Ireland, attended her own doctor during the antenatal period. No abnormality was noted and her blood pressure was, on average, 135/85. The expected date of delivery was 25th December, 1956.

She was admitted to a nursing home on 11th January, 1957, for medical induction and on 13th January, 1957, labour started. There was delay in the second stage and under open chloroform anaesthesia the patient was delivered by forceps, at the second attempt, of a live female infant weighing 9 pounds. This occurred at 23.30 hours on the 14th January. The delivery was difficult with deep perineal lacerations and the patient was shocked afterwards; the pulse was weak and thready and there was some bleeding from the uterus. At about 8 hours post-partum the systolic blood pressure was 60 mm. Hg and the patient was cyanosed. Intravenous therapy with dextraven, saline and blood was given, but the patient did not respond fully.

On the day following delivery the patient was febrile; this subsided with antibiotic treatment and, it is presumed, was due to a puerperal genital tract infection. On the 16th January, i.e., 2 days post-partum, systolic blood pressure was still 60 mm. Hg and the diastolic unrecordable. The patient was in a lethargic semi-confused state. At this time there was some hypogastric tenderness and rigidity was present to both right and left sides of the umbilicus. The uterus was contracted and there was no vaginal bleeding.

Over the next few days the patient improved slightly; the blood pressure readings on the 17th January are given as 94/50, 100/60, and on the 18th as 104/70.

At 6 days post-partum the patient collapsed again and remained in a moribund state despite treatment; the blood pressure was not obtainable. Nine days post-partum she was seen by one of us (J.B.F.) who found the patient conscious but with a pulse of 140 and a systolic blood pressure of 70 mm. She was dehydrated and tenderness was elicited over both kidney fossae. A diagnosis of adrenal insufficiency was made and 50 mg. cortisone given and repeated 6 hours later. Considerable improvement followed and the patient was transferred by ambulance to the Adelaide Hospital, Dublin. On arrival the patient was grossly dehydrated and its correction required about 5 litres of intravenous fluid during the first 24 hours in hospital. Treatment with cortisone, oral salt and antibiotics continued.

Eleven days post-partum the clinical chemistry figures were: sodium 137 m.eq./litre, potassium 4·9 m.eq./litre, chlorine 102 m.eq./litre and a blood urea of 431 mg. per cent. At the same time the blood haemoglobin was 11·1 g./100 ml., the haematocrit value was 34 per cent and the white cell count was 8,500 per c.mm. The urine was normal and the vaginal swab grew a pure growth of *Staphylococcus aureus*.

The clinical improvement seemed well maintained on 50 mg. cortisone daily but on the fourteenth post-partum day the patient again relapsed; the blood pressure was low, she was drowsy and "moribund", but the urine output was maintained. Recovery followed after 100 mg. of hydrocortisone had been given intravenously. A further and similar collapse occurred 3 days later and this too responded to intravenous hydrocortisone. After this date the daily dosage of cortisone was raised to 75 mg. together with 100 mg. deoxycorticosterone acetate by intramuscular injection. During the period from 12 to 20

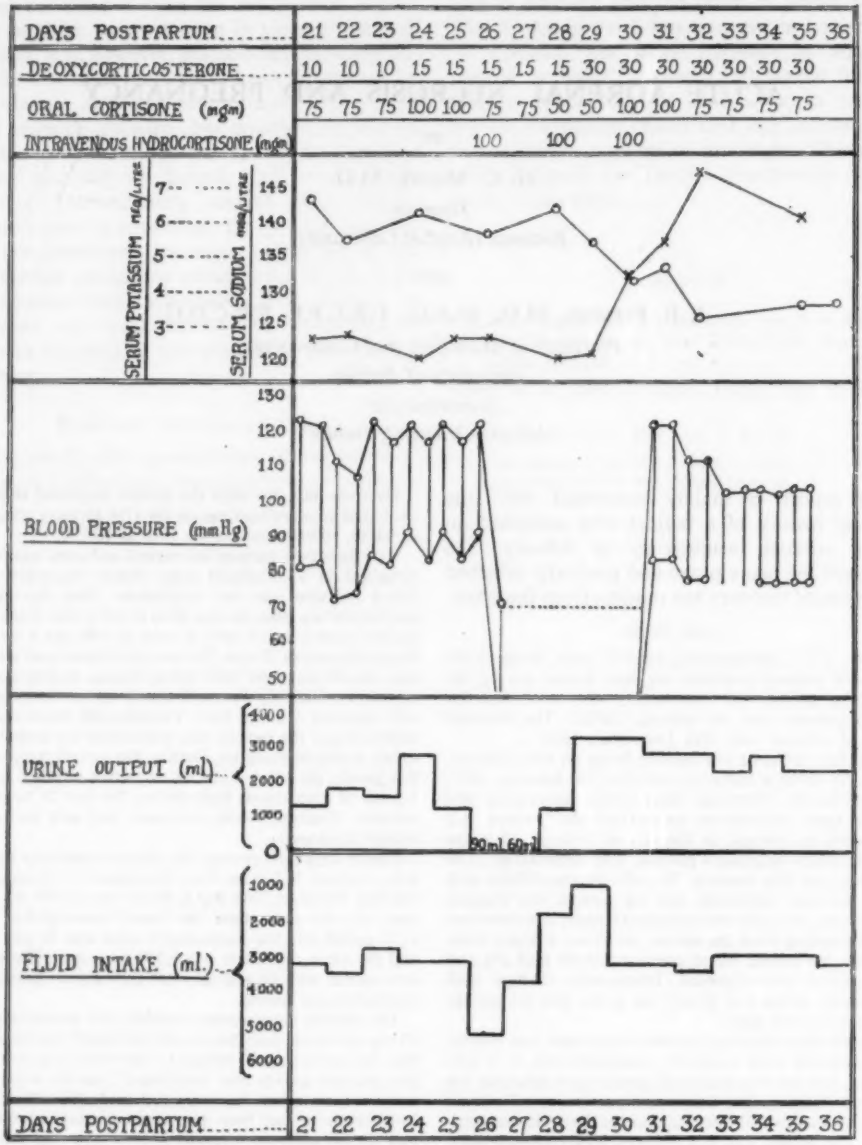
DAYS POSTPARTUM 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36
DEOXYCORTICOSTERONE 10 10 10 15 15 15 15 15 30 30 30 30 30 30 30
ORAL CORTISONE (mgm) 75 75 75 100 100 75 75 50 50 100 100 75 75 75 75
INTRAVENOUS HYDROCORTISONE (mgm) 100 100 100
SERUM POTASSIUM m.eq/Litre
SERUM SODIUM m.eq/Litre
BLOOD PRESSURE (mmHg)
URINE OUTPUT (ml)
FLUID INTAKE (ml.)
DAYS POSTPARTUM 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36
o——o Serum potassium. x——x Serum sodium.

FIG. 1

Progress of patient between 21st and 36th puerperal day. Blood pressure on days 27 to 30 is represented here by a dotted line (refer to text).

days post-partum great difficulty was experienced in the obtaining of blood samples and biochemical estimations were not carried out.

On the 21st puerperal day when blood was obtained the values were: serum sodium 123 m.eq./litre; potassium 6·7 m.eq./litre; chlorine 102 m.eq./litre; blood glucose 139 mg. and blood urea 459 mg. per cent.

Clinical and biochemical data for the period 21 to 36 days post-partum are given in Figure 1. The low serum sodium and high potassium values continued in spite of increasing the amounts of cortisone and deoxycorticosterone. On the 26th post-partum day a relatively sudden diminution of urine output was followed by collapse, the pulse rate rose and the blood pressure became unobtainable; her condition apart from oliguria was identical with the previous "collapses". During the next 4 days the patient's clinical state oscillated between collapse and relative recovery. The blood pressure (represented by the dotted line in Figure 1) varied widely during these days; was almost always low but rose occasionally to a systolic level of 110. There were three major episodes of collapse, although the patient was always very ill. Each of these episodes was treated by an additional 100 mg. intravenous hydrocortisone and was followed by a marked but transient recovery. Intravenous glucose saline as well as oral cortisone and deoxycorticosterone was maintained

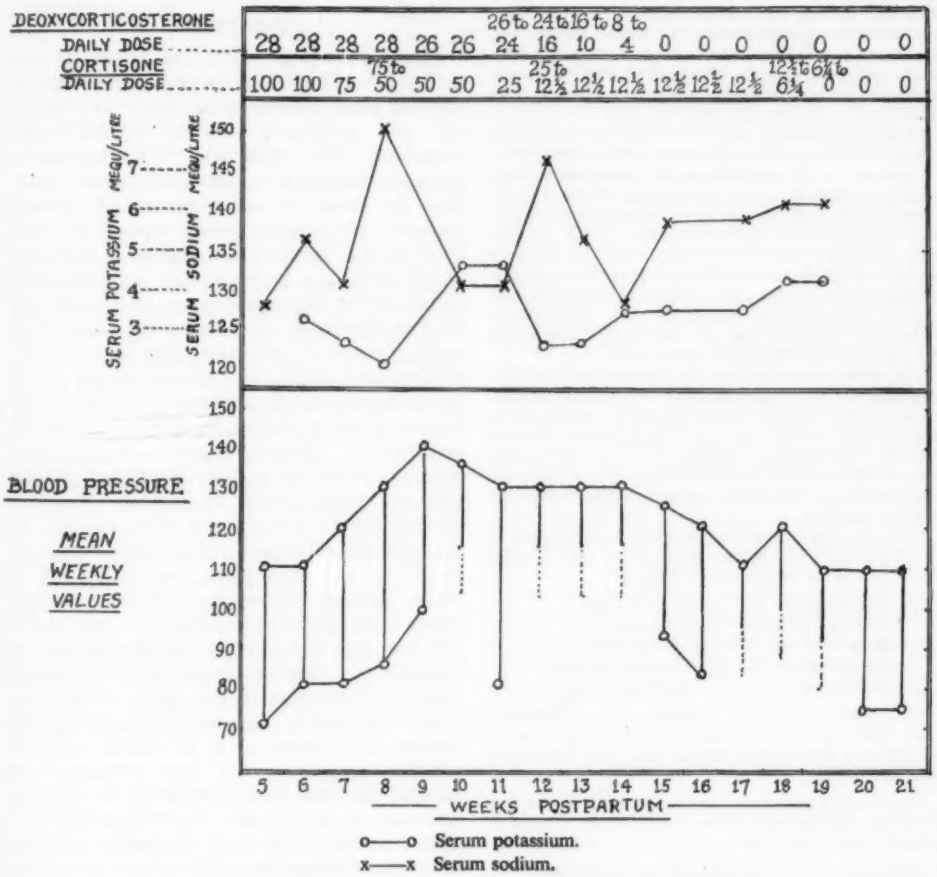
DEOXYCORTICOSTERONE DAILY DOSE
28 28 28 28 26 26 24 16 10 4 0 0 0 0 0 0 0
26 to 24 to 16 to 8 to
CORTISONE DAILY DOSE
100 100 75 75 to 50 50 50 25 25 to 12½ 12½ 12½ 12½ 12½ 12½ 12½ 6¼ 12½ to 6¼ to 0 0 0
SERUM POTASSIUM MEQU/LITRE
SERUM SODIUM MEQU/LITRE
BLOOD PRESSURE
MEAN WEEKLY VALUES
WEEKS POSTPARTUM
o—o Serum potassium.
x—x Serum sodium.

FIG. 2

Progress of patient from the 5th to the 21st puerperal week.

throughout the whole time. On other occasions during this period noradrenaline was given but its effect on the blood pressure was inconstant.

The urine output recovered on the 28th post-partum day, the electrolyte values reached relative normality 2 days later and the blood pressure reached 120/80 mm. Hg on the next day. At this time the cortisone dosage was 100 mg. per day and deoxycorticosterone was 30 mg. per day.

Almost coincident with the oliguria of this most recent collapse the patient sustained a urinary tract infection with *Escherichia coli* with high fever and leucocytosis. The blood urea level rose to 593 mg. per cent and at this time clinical hypocalcaemic symptoms occurred. The blood calcium level was 3·9 mg. per cent. The hypocalcaemic episode was treated successfully with intravenous calcium gluconate and oral calcium lactate. The urinary tract infection proved most resistant to antibiotic treatment and the temperature did not finally settle until about 4 months after delivery. There was no recurrence of the infection after this time.

Figure 2 summarizes most of the data for the period, 5th week to 21st week post-partum. During this period the amounts of deoxycorticosterone and cortisone were gradually reduced whilst maintaining added salt by mouth. There were two periods of relative hypertension, hypernatraemia and hypopotassaemia. These changes were presumably due to over-dosage. Since the patient's clinical condition remained relatively good the reduction in deoxycorticosterone and cortisone dosage still proceeded gradually and eventually was discontinued altogether. Additional salt by mouth was maintained but this too was eventually discontinued.

The blood urea returned to normal on the 47th puerperal day. The full clinical recovery was marred by a minor accident on 25th March, 1957 which resulted in an effusion into the right knee joint. This effusion became infected. The response to antibiotic therapy and aspiration was slow and the condition had not fully settled when the patient was last seen, about 7 months after the original accident.

Following the cessation of cortisone treatment and at about five and a half months post-partum the following blood and urine values were obtained:

(1) Serum sodium : 137 m.eq./litre
Serum potassium : 4·3 m.eq./litre
Serum chloride : 103 m.eq./litre
Serum calcium : 11·3 mg. per cent
Blood urea : 43 mg. per cent

(2) *Follicle stimulating hormone assay* (Klinefelter *et al.*, 1943): more than 6·6 units excreted every 24 hours. This finding supports the clinical view that there is no pituitary damage.

(3) *17-Ketosteroid assay* (through kindness of Dr. Bradshaw, Department of Physiology, Royal College of Surgeons): 2·8 mg. in 24 hours.

(4) *Kepler Test*: suggested adrenal insufficiency.

(5) Haemoglobin: 11·1 g./100 ml. Haematocrit: 36 per cent. Total white cell count of 8,550 per c.mm.

The patient was seen again six and a half months after delivery. She had remained quite well, her blood pressure was 115/90 and the serum biochemical values were within normal limits (sodium 143 m.eq./l., potassium 5·1 m.eq./l., chloride 103 m.eq./l., calcium 11·3 mg. per cent and blood urea 43 mg. per cent). Nevertheless the Kepler Test still disclosed evidence of adrenal insufficiency. The 24 hour 17-ketosteroid excretion remained at 2·8 mg.

At 10 months post-partum the Kepler Test and the electrolyte values were normal but the 17-ketosteroid excretion remained below average at 3·8 mg. per 24 hours. She was quite well apart from a recurrence of the swelling of the left knee.

Discussion

Many interesting points are raised by this incident. Not the least is the clinical relationship between acute adrenal insufficiency, i.e., necrosis, and pregnancy. Several reports (e.g., Crawford, 1951; Shearman, 1957) emphasize the many causative or associated factors which may be found in any instance of adrenal necrosis. Nevertheless when reports of fatal cases in the literature are studied a workable classification can be made out. An exhaustive survey of the literature has not been made but all the commonly quoted examples have been read; the one of particular importance is that of Crawford (1951). Five clinical groups are to be made out but the multiplicity of associated factors makes it difficult to ascribe a case with certainty to a particular group. In fact most instances of the association of adrenal necrosis and pregnancy occur in patients who are already suffering from some other disease, as, for example, eclampsia and accidental haemorrhage. On the other hand, there are a few in whom adrenal necrosis seems to be a primary event, in which the clinical picture is reasonably uniform and in which the symptoms may be regarded as directly caused by the adrenal necrosis. Consequently this group is of some importance and is discussed in detail under the heading of Group 1. It is indeed arguable whether pregnancy ever does predispose to adrenal necrosis, and particularly so since so few cases can be included. Nevertheless Group 1 seems to merit the title Idiopathic Adrenal Necrosis of Pregnancy.

All cases cited in all the groups were fatal. In fact, we are unaware of any proven instance

TABLE I
Clinical and Other Features of Fatal Cases of Acute Adrenal Necrosis of Pregnancy

Case and Author	Age	Parity	Gestation	Prior Antenatal State	Immediate Cause of Death	Symptoms and Signs						Duration Onset to Death	Adrenal Lesion
						Vomiting	Pain	Site of Pain	Fever	Purpura	Shock		
D.U.K., Keele and Keele, 1942	32	1	34	Normal	Aspiration of Mucus	+	+	Right side		Nil	Nil	10½ hours	Unilateral (Rt)
Arnold, Richer and Lepore, 1949	22	1	20	19 days before backache and urinary frequency		Nil	+	Right side	+	Nil	Nil	4 days	Unilateral (Rt)
Case 6: Crawford 1951	37	6	27	Normal		+	+	Epigastrium				2½ days	Bilateral
Case 7: Crawford 1951	40	5	Term	Normal	Aspiration of vomit	+	+	Left side			+	9 days	Bilateral
Peterson and Goldzieher, 1953	33	1	37		Paralytic Ileus	+	+	Right side				5 days	Unilateral (Rt)

of adrenal necrosis and pregnancy, other than the one recorded in the present paper, in which recovery is reported.

Group 1. Idiopathic Acute Adrenal Necrosis of Pregnancy

The details of the five members of this group are given in Table I. Prior to the actual onset of the disease the antenatal period is usually normal. At some time between the 20th week and term there is a sudden onset of abdominal pain with vomiting. The pain and tenderness, which are always present, are situated either in the epigastrium, or to one or other side of the uterus or umbilicus or in two or more sites simultaneously. There is usually no rigidity. The localization of the pain to one side of the umbilicus or to the other suggests that the ipselateral adrenal is affected, but this rule is not absolute. Shock only occurred once and this in a patient who was eventually proved to have bilateral lesions. Purpura is not recorded.

Probably the most important fact to be derived from Table I is that the disease is not necessarily fatal even when both adrenals are involved; 3 of the 5 cases died for reasons not directly attributable to adrenal necrosis.

Group 2. In Association with Shock and Haemorrhage

In the majority of cases which are included in this group there is sufficient reason for the shock state without necessarily invoking adrenal necrosis. Dystocia (Jeffcoate and Lister, 1952), rupture of an ectopic gestation (Margaret Hague Maternity Hospital, 1951), an incompatible or infected blood transfusion (Hurter, 1946) all feature as causes of the shock in many of the patients included here.

In other instances, however, the shock occurs for no obvious reason and at autopsy an adrenal necrosis is found. It is tempting to ascribe such a shock to the adrenal lesion but it should be emphasized that in the majority of instances of shock related to labour an adrenal lesion is not found at autopsy. During the last 5 years at the Rotunda Hospital 4 patients who died from shock have been studied. In 3 of these shock followed manual removal of the placenta and in the fourth shock followed a normal labour. In none was an adrenal lesion found. The relationship therefore between the shock state and adrenal necrosis is not at all clear.

Clinically, the patient may complain of pain which is distributed as in Group 1 cases. Frequently, however, the patient succumbs very quickly and no such history is given. Cases 2 and 3 of Dewhurst (1951) and Case 1 of Shearman (1957) are included here. Purpura occurred in Shearman's case but is not recorded by the others.

Group 3. In Association with Infection—Usually Abortion

Cases reported by Burnett (1948) and by Barry, Meagher and Geoghegan (1956) may serve as examples. In these, the patient collapsed suddenly following the abortion. Both of Barry's cases were cyanosed and purpura occurred in

one of them. Shearman's (1957) Case 3 is an example of puerperal sepsis associated with adrenal necrosis. Cases of this group are similar to those non-pregnant examples of adrenal catastrophe known as the Waterhouse-Friderichson Syndrome and it is presumed that infection occurred although this was not proved in any case.

Group 4. In Association with Other Distinctive Syndromes of Pregnancy

(a) *Vomiting of Late Pregnancy*. This particular association is described by Crawford (1951) and other cases are recorded by MacGillivray (1951). After a period of prolonged vomiting the patient suddenly collapses and dies. At autopsy bilateral lesions are found. Clinical data are lacking.

(b) *Eclampsia*, in which it is suggested there is an association of shock in eclampsia and the adrenal lesions. Figures vary widely. Way (1947) gave an incidence of 33 per cent in fatal cases of eclampsia. This is quite different from that of Crawford who gives a figure of 2·5 per cent. Other cases are recorded by Dewhurst (1951), and by MacGillivray (1951).

(c) *Accidental Haemorrhage*. In about 3 or 4 per cent of fatal cases, adrenal necrosis is found at autopsy (Sheehan and Moore, 1952). Other cases are recorded by Dewhurst (1951) and by MacGillivray (1951).

Group 5. In Association with Conditions Incidental to Pregnancy

Dodds (1945) recorded a case in which the primary condition was a hepatic necrosis and it is thought that the adrenal haemorrhage was part of a general bleeding diathesis.

Pathology. The standard report on the pathology of adrenal necrosis in pregnancy is that of Crawford (1951). Of her 14 cases 2 have been placed here in Group 1 and the remainder are distributed throughout the other groups and sub-groups. She assumed that the pathology was the same in all cases, i.e., necrosis and haemorrhage, either multiple focal lesions or massive destruction. A fibrinoid necrosis of capillary walls is also described but Crawford maintains that this change is secondary to the necrosis. The question of thrombosis of the central vein is also raised since such a thrombosis has been described as a causative factor. It would seem that adrenal necrosis and central vein thrombosis are not necessarily interdependent; an analysis of the cases of the groups proposed here does not give a definite answer on this point largely because of inadequate autopsy information.

The precise cause of the adrenal lesion remains unknown although dietary deficiencies, infection and vascular disturbances have all been suggested.

The Present Case

The case reported here belongs to the clinical Group 2. The surprising fact of her survival for 9 days without specific steroid therapy should be emphasized, particularly since the bilateral character of the abdominal tenderness would suggest a bilateral adrenal lesion. It is also somewhat surprising that the patient's electrolyte values remained normal for at least 11 days following the onset in spite of the fact that cortisone was not given until the 9th day post-partum.

It is known that "crises" may occur both when the electrolytes are normal and when the electrolytes show the characteristic imbalance of adrenal insufficiency. Shearman (1957) reviews the two types of collapse and describes clinical differences. The patient reported here sustained both types of adrenal crisis but clinically the attacks seemed to be similar and it is not known whether the oliguria of the last attack (Fig. 1) is peculiarly associated with the electrolyte abnormalities or more simply related to the hypotension.

That uraemia may occur with an acute adrenal insufficiency is well described and is thought to be due to an increased cell catabolism as well as to a lowered glomerular filtration rate (Nabarro, 1956). Another biochemical abnormality of importance was that of hypocalcaemia. At the time this was noted the patient had a urinary tract infection. Nevertheless it is thought unlikely that the renal condition could be held responsible since there is no evidence of prolonged renal insufficiency. It is more probable that the hypocalcaemia was due to cortisone therapy since it is known that this may produce a negative calcium balance and

possibly tetany (Goodman and Gilman, 1955).

Probably the most important lesson to be derived from the present case concerns treatment. When the diagnosis of acute adrenal insufficiency was made on the 9th puerperal day a daily dose of cortisone of between 50 mg. and 100 mg. was given by intramuscular injection. This dose was clearly inadequate to sustain her, electrolyte abnormalities occurred and further attacks of acute adrenal insufficiency supervened. These attacks required both intravenous hydrocortisone and deoxycorticosterone acetate (Fig. 1). Consequently it occurs to us that any case of adrenal necrosis of or in pregnancy, and especially if judged to be bilateral, should receive intravenous hydrocortisone or α fluorohydrocortisone in a dosage similar to that suggested by Hart (1957) for the acute Addisonian crisis, i.e., up to 300 mg. of intravenous hydrocortisone per day or 1/20 of this if α fluorohydrocortisone is to be used. Furthermore in the present case two episodes of overdosage occurred (Fig. 2) and the amount of cortisone could have been reduced as soon as the patient was stabilized clinically with a reasonably normal blood pressure. This state of affairs was reached at about 6 weeks postpartum and cortisone could have been reduced much more quickly.

Post-partum Addison's Disease

That a patient may recover fully from an acute adrenal necrosis in pregnancy is clear from the present report. Nevertheless the possibility, in similar cases, of subsequent chronic adrenal insufficiency, i.e., Addison's disease, should be borne in mind particularly in those instances in which the original lesion is a massive destruction. Whether a significant proportion of women with Addison's Disease have had such a catastrophe to explain the chronic adrenal insufficiency seems to be doubtful. This possibility was raised by Crawford (1951) to explain the reported female preponderance in Addison's Disease; she gives figures of female/male ratios varying between 6:1 to 16:1. However Sloper (1955), in an analysis of nine cases of Addison's Disease in women due to "atrophic adrenals", found that there was no history of a previous acute episode in any of them.

Summary

Following a difficult delivery with shock, a patient suffered from an acute adrenal insufficiency due, presumably, to a necrosis. She recovered from the acute attack and, after a period of several months during which evidence of adrenal insufficiency could still be found, she made a full clinical recovery 10 months after the onset. At this time the biochemical values were normal with the possible exception of the 24-hour 17-ketosteroid excretion which remained below average.

The association of adrenal necrosis with pregnancy is discussed and a scheme of classification suggested.

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A RADIOLOGICAL SURVEY OF THE FEMALE PELVIS IN UGANDA

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WITH ADDENDUM ON THE MEASUREMENTS OF SPECIMENS OF THE FEMALE BONY PELVIS

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IT is now generally accepted that radiology offers the most accurate method of assessing the pelvic size in the living subject. As the result of X-ray pelvimetry, Heyns (1946) in South Africa, and Thoms (1946) and Torpin (1951) with many others in America, have shown that the coloured peoples have a smaller pelvis than the white population. No previous survey has been made on the pelvis of the Uganda African, although in 1938 (Mitchell, 1938; Cook, 1938; Stones, 1938) there was a short controversy in the medical press as to whether the pelvic brim was generally contracted or flat.

THE MATERIAL

The present investigation was made at Mulago Hospital, Kampala, on patients attending the antenatal clinics, apart from 5 patients who were X-rayed after delivery. The patients who were sent for pelvimetry were chosen solely because they lived moderately near the hospital, and the X-rays were taken when the patients were thought to be about 36 weeks. X-ray pelvimetry was carried out on 105 patients of whom 77 were Ganda and 13 belonged to other closely associated Lacustrine Bantu tribes. The remaining 15 were a very mixed group, so that the results presented here are only those of the Bantu tribes. The parity of the patient was recorded in only 77 cases but of these 41 were multiparae and 36 primigravidae.

THE INVESTIGATION

The height of each patient was measured against a foot-rule fixed to the wall of the clinic.

Three X-ray films were taken of each patient. The brim view was taken with the patient reclining so that the pelvic inlet was parallel with the table top. The lateral view was taken with the patient in the erect position with a half centimetre scale placed between her thighs. The outlet view was taken by the Chassard Lapine technique as described by Van Herik and Good (1950), the patients finding singularly little difficulty in assuming the required squatting position.

From the lateral view the antero-posterior diameter of the brim (true conjugate) and of the outlet were measured. The transverse diameter of the brim and the bispinous diameter were measured on the brim view and the subpubic angle was measured by Nicholson's technique (1938) on the outlet view. Finally, in order to compare the results more fully with those from

the department of anatomy the straight sacral height and the depth of the symphysis pubis were measured on the lateral film.

As far as possible the subsequent course of pregnancy was followed, but unfortunately only 51 patients were delivered in hospital.

TABLE I

The Pelvic Brim

Measurement	Origin	Mean	Standard Deviation	Coefficient of Variation	Range
True Conjugate (cm.)	Uganda Bantu ..	9·97	0·85	8·6	8·1 – 11·8
	South African Bantu	10·59	0·81	7·7	8·2 – 12·5
	Rural England ..	11·64	1·05	9·0	8·35– 14·35
	London	11·83	1·0	8·5	8·7 – 15·0
Transverse Diameter of Brim (cm.)	Uganda Bantu	11·2	0·75	6·6	9·4 – 13·4
	South African Bantu	11·34	0·80	6·9	9·15– 13·0
	Rural England ..	13·23	0·76	5·8	11·0 – 16·0
	London	13·06	0·7	5·4	10·9 – 15·4
Area of Brim (sq. cm.)	Uganda Bantu ..	87·2	10·11	11·6	63·7 –119·9
	South African Bantu	99·33	12·09	12·2	66·6 –127·6
	Rural England ..	121·0	12·9	10·7	86·0 –162·0
	London	126·8	12·8	10·1	95·0 –165·0
Brim Index	Uganda Bantu ..	87·6	7·85	9·0	65·18–107·84
	South African Bantu	93·6	7·20	7·7	79·7 –121·2
	Rural England ..	88·3	9·40	10·7	65·5 –113·5
	London	90·8	8·20	9·1	64·0 –115·0

A comparison of the Uganda Bantu pelvis with the South African Bantu and the Rural and Urban British pelves.

TABLE II

The Mid-Pelvis and Outlet

Measurement	Origin	Mean	Standard Deviation	Coefficient of Variation	Range
Bispinous Diameter (cm.)	Uganda Bantu ..	10·0	0·67	6·7	8·2 – 11·7
	South African Bantu	10·47	0·93	8·9	7·45– 12·58
	Rural England ..	10·54	0·77	7·3	8·25– 12·75
	London	9·95	0·71	7·1	7·5 – 11·5
Pubo-sacral Diameter (cm.)	Uganda Bantu ..	11·03	0·72	6·6	9·2 – 13·3
	South African Bantu	12·20	1·33	10·9	9·1 – 15·7
	Rural England ..	13·01	0·96	7·4	10·3 – 16·0
	London	11·97	0·86	7·2	9·5 – 14·5
Area of Outlet (sq. cm.)	Uganda Bantu ..	85·57	10·52	12·3	61·98–115·32
	South African Bantu	100·12	15·12	15·1	64·5 –131·0
	Rural England ..	106·7	11·90	11·2	76·0 –142·0
	London	93·7	10·40	11·1	65·0 –120·0
Subpubic Angle (degrees)	Uganda Bantu ..	78·1	7·5	9·6	64 – 95
	Rural England ..	84·8	7·3		

A comparison of the Uganda Bantu pelvis with the South African Bantu, the Rural and Urban British pelves.

TABLE III

Type of Inlet According to Thoms's Classification

	Dolichopellic Per cent	Mesatipellic Per cent	Brachypellic Per cent	Platypellic Per cent
Uganda Bantu	10·2	28·4	58·0	3·4
Chinese (Wei, Chen and Chen, 1956)	20·7	35·3	41·7	2·3
Filipino (Manahan, Marquez and Mangay, 1954) ..	27·3	42·5	29·2	0·5
American Negro (Thoms, 1946)	29·0	43·0	25·0	3·0
American White (Thoms, 1946)	22·6	46·6	28·8	2·0
American White (Roth, 1953)	6·6	32·4	54·4	3·9

RESULTS

The results presented here are those of the 90 patients belonging to the Ganda and other Bantu tribes. It was found, as was to be expected, that there was close agreement between these two groups.

In Tables I and II the results are compared with those of the South African Bantu (Heyns, 1946), the rural English figures of Nicholson (1938) and the London figures of Ince and Young (1940).

It will be seen that the pelvic brim is smaller in all dimensions than even the South African Bantu. The mean area of the brim falls just below the figure of 90 sq. cm. which Nicholson (1938) claims to be the critical degree of brim contraction. The brim index of 87·6 is indicative of a round or gynaecoid brim and in the whole series only 3·4 per cent could be classified as platypellic according to Thoms's definition (1939). Table III compares the Uganda results with those of several other racial types and confirms that the gynaecoid brim is the most usual type. The figures are almost identical with those of the white American female series of Roth (1953), the small number of dolichopellic pelves being the most noticeable feature.

The mid-pelvis and outlet show less divergence from the other three series of X-rays (Table II). The outlet area is calculated from the bispinous diameter and the pubo-sacral diameter and although 85·57 sq. cm. is the smallest area recorded there is a much smaller difference than in the area of the brim. It is fully realized that a measurement of the subpubic angle does not give a complete measurement of the fore-part of the pelvic outlet, but it was felt that it was a useful indication of the pelvic shape and it was a measurement which could be directly compared with the anatomical data. That the British figure for the subpubic angle was 84·4 degrees, which agrees with the Australian figure of 83 degrees of MacDonald and Thomas (1953), was more surprising than that the subpubic angle of the Bantu pelvis was 78·1 degrees.

The mean height of the patients X-rayed was 5 feet ½ inch with a range of 4 feet 4 inches to 5 feet 4 inches. The mean height of the symphysis pubis was 3·4 cm. and the straight height of the sacrum was 9·5 cm. Berman (1955) states that the American white woman has a symphysis pubis of 4–6 cm.

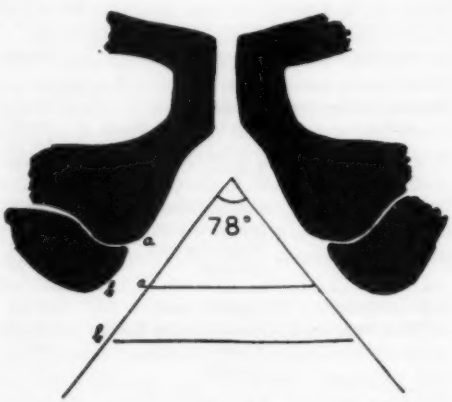

FIG. 1

Subpubic angle showing Bantu pelvis superimposed on European pelvis.

Discussion

To anyone with clinical obstetrical experience among the Bantu in Uganda the results were not surprising, apart from the measurement of the subpubic angle which was greater than was expected. The explanation for this is to be found in the overall size of the pelvic bones which are much smaller than those of the European. The obstetrician estimates the size of the outlet clinically from the bi-tuberous diameter. From Figure 1 it will be seen how the decreased length of the ischio-pubic ramus will give the impression of a much smaller outlet to an obstetrician who is used to working among Europeans. The angle subtended by a given bi-tuberous diameter is dependent on the length of the ischio-pubic rami, therefore if the rami are short the angle will be greater than anticipated and consequently the foetal head will be able to lie farther forwards as it emerges through the outlet.

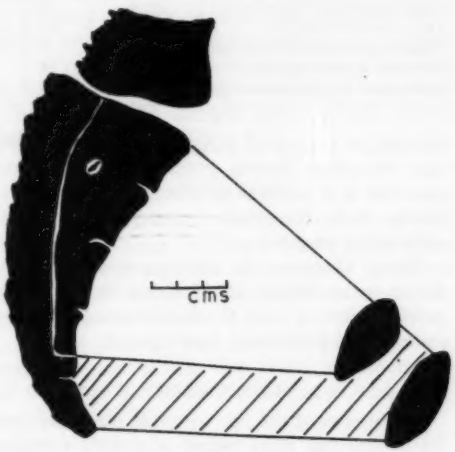

Fig. 2

Lateral view of pelvis showing Bantu pelvis superimposed on European pelvis.

Figure 2 shows the lateral view of the pelvis superimposed on that of a European. The extreme shallowness of the Bantu pelvis is important for it is probably owing to this factor that labour so often ends in a normal spontaneous delivery. It is interesting to note that as a result of this shallowness of the pelvis the pelvic organs are very easily palpated on vaginal examination and the pregnant uterus is palpable per abdomen 4 weeks earlier than it is in the European.

The pelvic bones are not disproportionally small compared with the rest of the skeleton, and this is shown by the average height of the patients which was only 5 feet ½ inch. Bernard (1952) compared the X-ray pelvimetries of tall women with those of small women in Scotland. His small women were all under 5 feet in height. Table IV shows the measurements of his small

Table IV

A Comparison of Bernard's Small Women with the Uganda Bantu

	True Conjugate (cm.)	Brim Area (sq. cm.)	Brim Index
Uganda Bantu	9·97	87·2	87·6
Scotland (small women under 5 feet)	10·77	106·8	85·1

women compared with those of the Bantu pelvis. The latter are still smaller although the difference is not so great. Bernard found that a small pelvis was more common among women from the lower social grades. Under the conditions in which the present investigation was made, it was not possible to assess the social status of the patients but it would be interesting to see if those patients who had had an adequate diet from infancy had larger pelves. If this were so it suggests that the problem of disproportion will decrease in the next few years, as the standard of living rises among the people of Uganda.

In discussing the problem of disproportion the size of the foetus is important, so this was investigated at the same time. It is hoped that the results of this investigation will be published in full at a later date. It was found that the Bantu foetus has an average weight at birth of between 6½ and 7 pounds. This is only a few ounces less than that of the full-term foetus in Britain (Ellis, 1951).

In view of the small average size of the pelves and the relatively large foetuses, a high incidence of operative deliveries would be expected but it was found over a period of 4 years that 85 per

cent of all deliveries in hospital were spontaneous. Of the 90 patients X-rayed only 44 were delivered in hospital, but it can be fairly safely assumed that those not returning for delivery were spontaneously delivered at home. If the 5 cases who were X-rayed after delivery (2 craniotomies and 3 Caesarean sections) are excluded, there were 6 Caesarean sections, 5 forceps deliveries and one craniotomy in 85 deliveries, an incidence of 14·1 per cent operative deliveries. This low incidence of operative deliveries without an increase in the length of labour makes it probable that the Bantu uterus acts more efficiently than the European uterus. So far it has not been possible to prove this but it is an impression held by most clinicians with experience of obstetrics in Uganda. However, the incidence of operative deliveries in the patients X-rayed is comparable with that of the total admissions and shows that this series is representative of all the cases admitted to hospital.

Addendum on the Measurement of Specimens of Female Bony Pelves

Thirty-one dried and disarticulated bony pelves were examined from adult female cadavers. Their source was from Lacustrine Bantu tribes inhabiting the northern shores of Lake Victoria (Ganda, Toro, Soga, Rwanda).

Method

For the purpose of checking the measurements obtained by X-ray pelvimetry two absolute lengths were measured on individual bones. These were the height of the symphysis pubis, estimated by measuring the exposed articular surface on one innominate bone, and the straight sacral length measured between the anterior lips of the first and last sacral segments. The bony pelvis was then articulated as accurately as possible, using plasticine as an adhesive substitute for articular cartilage.

The following measurements were made on each pelvis: (1) conjugata vera, (2) transverse of brim, (3) interischial spine diameter, and (4) antero-posterior of the outlet (from lower border of the symphysis pubis to the anterior tip of the sacrum). (5) The subpubic angle was estimated with perspex calipers after the technique of Nicholson (1938). From these measurements the brim area, brim index, and outlet area, were calculated. It is not likely that these latter measurements will have the same accuracy as those on single bones because the thickness of plasticine in the pelvic joints must necessarily be an approximation to that of the articular cartilage in the "green" pelvis. To test this factor measurements on a "green" articulated pelvis were compared with those on the same pelvis after processing and re-assembly with plasticine. The results shown in Table V demonstrate a reasonable degree of congruity. One concludes that distortion during preparation is minimal and that it is justified to compare the measurements made on dried re-assembled skeletons with living material.

Table V

Pelvic Skeletal Measurements of MC337

	Green Articulated	Dried Re-articulated
Total height (cm.)	21·2	20·9
Intercristal diameter (cm.) ..	25·4	24·9
Interspinous diameter (cm.) ..	21·45	21·0
Anteroposterior diameter (cm.)	10·4	10·7
Transverse of inlet (cm.) ..	12·3	12·5
Height of symphysis pubis (cm.)	4·5	4·4
Subpubic angle (degrees) ..	65	74
Interischial spine diameter (cm.)	9·4	9·7

Table VI compares the figures obtained by direct measurement of 31 dried re-articulated pelvic skeletons with those calculated from the radiological pelvimetry investigation.

Conclusions

The means of the two absolute measurements on articulated bony pelvic skeletons (straight sacral length and height of the symphysis pubis) are practically identical with the same measurements in the series of X-ray pelvimetries. The means of the outlet measurements and the subpubic angle are also strikingly similar in the two series. The conjugata vera also shows the same congruence. The transverse of the brim is however rather larger in the osteological series, and this similarly affects the brim area. The reason for this (which is in line with other investigators' findings, Heyns, 1947), is that the shadow taken

TABLE VI

Comparison of Osteological and Radiological Data

	Osteological Data (31 cases)			Radiological Data (90 cases)		
	Mean	Range	S.D.	Mean	Range	S.D.
Conjugata vera (cm.) ..	10·3	12·4– 8·3	0·96	9·97	11·8 – 8·1	0·85
Transverse brim (cm.) ..	11·8	13·3–10·3	0·74	11·2	13·4 – 9·4	0·75
Brim area (sq. cm.)	97·8	129·5–73	12·2	87·2	119·9 –63·7	10·11
Brim index	87·3			87·6		
Interischial spine length (cm.)	10·0	11·4– 8·3	0·81	10·0	11·7 – 8·2	0·67
Pubo-sacral length (cm.) ..	11·1	13·3– 9·6	0·60	11·03	13·3 – 9·2	0·72
Outlet area (sq. cm.) ..	84·5	116·9–66·0	12·3	85·57	115·32–61·98	10·5
Subpubic angle (degrees) ..	79·5	102 –60	11·5	78·1	95 –64	7·5
Straight sacral length (cm.)	9·7	13·0– 8·0	0·68	9·5	12·2 – 7·3	0·81
Symphysis pubis height (cm.)	3·2	4·1– 2·4	0·7	3·4	4·3 – 2·8	0·32

as the brim on X-ray pelvimetry is in fact a little below the iliopectineal line and therefore rather nearer the midline, thus giving a slightly shorter transverse diameter and smaller brim area than is actually present. Ranges and standard deviations are also of the same order in both series.

The osteological investigation therefore fully confirms the accuracy of the estimations obtained in the sample used in the X-ray pelvimetry investigation.

SUMMARY

X-ray pelvimetries were performed on 105 patients attending Mulago Hospital, Kampala. Of those 105 patients 90 belonged to Bantu tribes and the results of the pelvimetries on these patients are reported.

It was found that the Bantu pelvis was generally contracted. The mean measurements of the main diameters are compared with other published surveys.

The clinical significance of this contracted pelvis is discussed with a note on foetal size and method of delivery.

The radiological data are compared with those of dry bone material.

ACKNOWLEDGMENTS

We wish to thank Dr. Davies and the radiographers at Mulago Hospital for their help with this investigation and to record our gratitude to Professor Rendle Short who gave us so much encouragement while this work was in progress.

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INCREASED PETHIDINE DOSAGE IN OBSTETRICS ASSOCIATED WITH THE USE OF NALORPHINE

BY

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PETHIDINE fulfils many of the ideal qualities of an analgesic for the first stage of labour, and this is reflected in its widespread popularity and use. In common with other drugs, however, its chief drawback has been the production of foetal respiratory depression when it has been given in any appreciable amounts to the mother. Therefore, the amounts usually advocated in obstetric practice have been restricted to between one and two hundred mg. Thus, Josephine Barnes, who in 1947 reported on 500 cases, found that the majority received 100 mg. and only 32 received more than 200 mg. The production of foetal anoxia in this range of dosage is unlikely to be of any consequence. However, many would agree with Chalmers and Thornberry who, writing on this problem in 1954, stated ". . . there are many types of case in which a greater freedom in the use of sedatives is an advantage, which is available only when we know that respiratory depression in the foetus can satisfactorily be antagonized". They were discussing the use of the drug N-allylnormorphine in the treatment of neonatal asphyxia due to the use of pethidine and/or morphia. The action of this drug (also known as nalorphine and sold as Lethidrone), has now been clearly established, and it would appear to be the "satisfactory antagonist" to which Chalmers and Thornberry were referring. They themselves describe its efficacy in cases of pethidine dosages during labour in the range of 300–400 mg., and refer to this amount as being "heavy sedation".

It has been felt for some time that with the use of nalorphine the amount of pethidine given during the first stage could well be increased, providing greater comfort for the mother, and without prejudicing the safety of the baby. It seemed to be particularly indicated in those cases in which the labour was prolonged, or where the mother found smaller doses ineffective in producing adequate analgesia. Accordingly over the years 1954, 1955 and early 1956, a clinical trial was made with this end in view.

MATERIAL

Three hundred labours were studied in which all the mothers were primigravidae and all of whom received 400 mg. of pethidine or more. These patients formed almost exactly one-third (32 per cent) of the primigravidae delivered at St. Mary's during these years. Forty-six per cent of the other primigravidae needed only 200 mg. of pethidine and the remaining 22 per cent were comfortable with milder sedatives or found the help given by the relaxation classes, run by the Physiotherapy Department, sufficient for their needs. Whereas nalorphine is also effective in preventing respiratory depression when morphia has been used, for the sake of simplicity we concentrated entirely during these years on pethidine. For a similar reason scopolamine was

not used either, although its value in association with pethidine is appreciated.

In the selected cases studied, the following points were recorded:

(1) The method of delivery.

(2) The duration of the first and second stage.

(3) The amount and time that the pethidine was given.

(4) Any side effects due to this drug.

(5) The amount and nature of any post-partum haemorrhage.

(6) The condition of the foetus at birth.

Assessing this latter factor is notoriously difficult and presented the biggest problem. The exact measurement by a trip spirometer of the respiratory minute volume of the infant after birth as used by Donald and Lord (1953) and Roberts *et al.* (1957) has much to commend it. Cross (1949) has used a plethysmograph, which is probably more accurate, to measure the minute volume, and at present a further trial is being organized in the Department with this added refinement. It is felt, however, that there is more to the assessment of asphyxia than a measurement of the respiratory exchange of the foetus by itself. Agpar's (1953) clinical assessment of foetal respiratory depression, expressed over a numerical range, appeared too complex and more reliance was placed on a classification akin to Flagg's (1944), dividing the degree of anoxia into severe, moderate and mild. A severe case would be one in which the infant was markedly asphyxiated with poor muscle tone and needed intensive resuscitation which had to be continued for fifteen minutes or over. The phrenic stimulator, together with intra-gastric oxygen, was the usual method. A moderate case would be when a baby was clinically less asphyxiated, but required definite resuscitative methods such as the above for up to 15 minutes. A mild one was an infant which showed evidence of definite asphyxia, but required only oxygen and pharyngeal toilet to regain normal vigour and respiration within 5 minutes.

Three cases in which there were gross congenital abnormalities of the foetus incompatible with life were excluded from this series.

Method and Times of Dosage

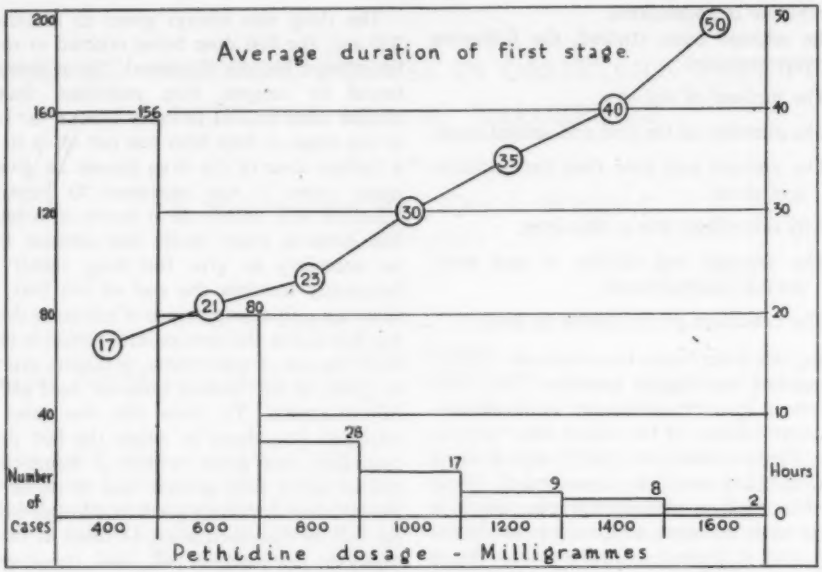
The drug was always given in amounts of 200 mg., the first dose being injected as soon as the patient became distressed. No evidence was found to suggest that pethidine decreases uterine contractions in early labour, or indeed at any stage. A time limit was not set as to when a further dose of the drug should be given. In many cases it was necessary to repeat the injection well before the 4 hours so arbitrarily laid down in many books had elapsed. It may be necessary to give the drug rather more frequently towards the end of the first stage, since not only does a degree of tolerance develop, but this is also the most painful period in labour. With the use of nalorphine, pethidine can safely be given to the mother however near she is to full dilatation. To show this the cases were analyzed into those in which the last dose of pethidine was given within 2 hours of the patient being fully dilated, and those in which the last dose had been given at a longer interval. As will be described later, 11 cases of neonatal asphyxia occurred in all, and these will be analyzed in some detail. However, their distribution in relation as to when the last dose was given did not suggest that this factor was of any significance, provided, of course, that nalorphine had been used.

Table I

Last Dose/Full Dilatation Interval	Number of Cases	Asphyxia Cases	
2 hours or less ..	104	3	Severe 0 Moderate 2 Mild 1
More than 2 hours	196	8	Severe 1 Moderate 2 Mild 5

Nalorphine can either be given intravenously to the mother (the usual dose being 10 mg.), or can be injected into the umbilical vein of the baby (0·25 mg. being the normal amount). Again, to keep the number of variables as low as possible, nalorphine was given routinely in this series to the mother, the average time being 5 minutes before delivery was expected, and the

TABLE II



amount 10 mg. It can be argued that some of these babies might not have been born under the effect of pethidine, and that the nalorphine could have been saved for those that were definitely "pethidinized". It was felt, though, that it was advisable to prevent the onset of such a potentially dangerous condition as neonatal asphyxia, particularly since giving an injection into the umbilical cord vein may not always be easy and quick.

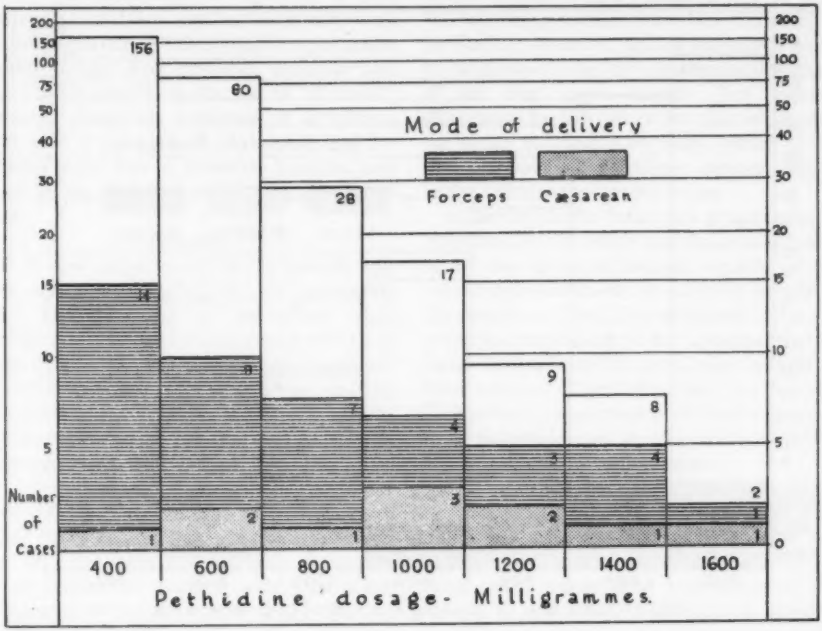
RESULTS

The dose distribution is shown in Table II and superimposed on this is the average duration of the first stage.

These two factors have been plotted against each other to show how, in the main, larger doses have been necessary in cases of prolonged labour (usually due to uterine inertia). It is a feature of these patients that their uterine contractions are extremely painful, and if this ordeal is going to be prolonged up to 36 or 48 hours, or even longer, it is a great advantage to be able to make this time as comfortable as possible. The overall incidence of prolonged labour in primiparae during the years under study was 4·2 per cent (taking 48 hours or more as the standard) and this is in line with other figures taken from teaching hospitals: 3·2 per cent (MacRae, 1949, Queen Charlotte's Hospital); 7·6 per cent (Nixon, 1948, University College Hospital). While it is agreed that a large proportion of the prolonged labours did occur in the pethidine series, this is to be expected, and it was not felt that these mothers were having a prolonged labour because of the high pethidine dosage. This is substantiated by the fact that the overall inertia rate during these years was not abnormally high. By a similar argument it cannot be supported that full sedation with pethidine decreases the likelihood of inertia.

Mode of Delivery. Fifty-one mothers were delivered by forceps, giving an incidence of 17 per cent. There is no doubt that this would appear at first to be rather high, but it should be remembered that not only were these patients all primigravidae, but also that they were a selected group containing a high percentage of abnormal

TABLE III



cases. The relationship between the amount of pethidine given and the incidence of forceps delivery is shown in Table III.

It can be seen that the mothers who had had a large amount of pethidine had a high incidence of instrumental deliveries, and this is not denied. It does not mean, however, that this occurred because the mother was too drugged to co-operate in the second stage, but rather that it was often felt expedient in these prolonged labours to shorten the second stage. This is in accordance with most modern opinion, and Jeffcoate (1953) refers specifically to this point.

Eleven patients were delivered by Caesarean section giving an incidence of 3·6 per cent. The distribution of these cases relative to the dosage of pethidine is also shown in Table III. Out of the 11, 5 were performed to terminate an inert labour. One was for a brow presentation, 3 for a failed trial of labour, and 2 for foetal distress alone.

There was one breech delivery in which the mother received 600 mg. of pethidine.

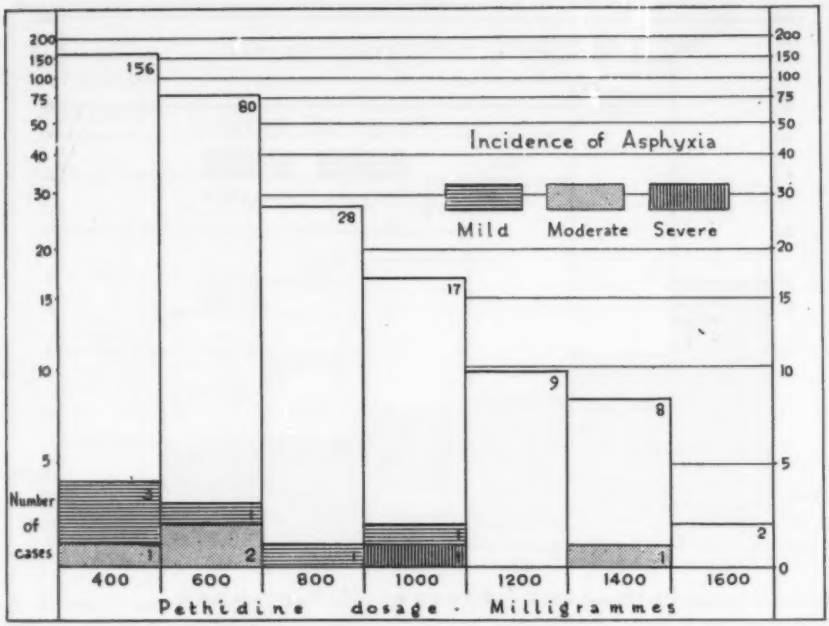
Incidence of post-partum haemorrhage. Accepting the standard definition of twenty ounces, this occurred 18 times, giving an incidence of 6 per cent in these 300 cases. The distribution of this group relative to the dose given is shown in Table IV.

It would not appear that increased dosage with pethidine bears any relationship to the incidence of post-partum haemorrhage.

TABLE IV

Number of cases	156	80	28	17	9	8	2
Post-partum haemorrhage	11	4	2	1	—	—	—
Pethidine dosage (mg.)	400	600	800	1,000	1,200	1,400	1,600

TABLE V



Side effects due to pethidine. Vomiting, which after all is often a feature of normal labour, was very occasionally troublesome when larger doses of pethidine were being used. No other side effects such as vasomotor collapse or respiratory depression, which had been reported by other workers, were noted in this series.

Incidence of asphyxia. The difficulty of assessing this critically has already been discussed. Eleven of the babies born showed a significant degree of asphyxia. The degree of this and its relationship to the amount of pethidine is shown in Table V.

The severely asphyxiated baby was born after a forceps delivery under general anaesthesia for foetal distress, the mother having mild pre-eclamptic toxaemia and the first stage having lasted 34 hours. Respiration was only established after 35 minutes. A 1,000 mg. dosage of pethidine had been given during the labour and the nalorphine injected as soon as the mother was anaesthetized. It is obviously almost impossible in this sort of case to apportion the blame for the asphyxia.

In the 4 moderate cases, 2 were again delivered under general anaesthesia by forceps. The other 2 were normal deliveries and, although the asphyxia was marked, the babies clinically did not appear "pethidinized" and were quite vigorous once respiration had become established. Two of the mild asphyxias had been delivered by Caesarean section and one by forceps.

Two stillbirths occurred, one of which was due to an error of judgment, the baby being delivered with considerable difficulty by forceps, and post mortem was found to have a tentorial tear. The other was again after a forceps delivery for foetal distress which developed during the second stage. The first stage had lasted 26 hours, and the mother had received 800 mg. of pethidine. The baby's heart was beating just prior to delivery, but respiration was never established. There was a tight true knot in the cord to which it was felt that the asphyxia and resultant stillbirth might reasonably be attributed.

The overall percentage of asphyxia is thus 3·7 per cent, and this compares favourably with the figures reported in other trials on pethidine or similar drugs. For example, Roberts and Wrigley (1953) describing the use of "Nisentil" in obstetrics found an incidence of significant asphyxia of 6·5 per cent. It is also felt that the 2 stillbirths were due to obstetric hazards, and were not in any way connected with the use of pethidine.

Discussion

There is now ample proof of the specific and efficient action of nalorphine in preventing neonatal asphyxia due to pethidine. Thus Eckenhoff, Hoffman and Funderburg (1953), in studying over 1,000 cases, found a significant reduction in the need for resuscitation and the time required to gasp and breathe in the infants, when nalorphine had been given, compared with the controls, in which saline had been used. The dose of pethidine they used, however, never exceeded 400 mg. Barr and Barr (1956) have also described the good results to be expected from the use of nalorphine and in their discussion state: "At present the value of nalorphine is not that it permits of indiscriminate administration of morphine and pethidine to all parturients, but rather that it allows these narcotics to be employed with greater confidence in cases where they are considered necessary." While this is entirely endorsed, it is our contention that the greater confidence felt by the obstetrician should result in more complete analgesia for the mother when this is necessary and this clinical trial was designed with this end in view.

Some of the problems in assessing the effects of a drug used in obstetrics have been mentioned, but, in common with other workers, we found two factors to be particularly difficult to analyze. These were, firstly, a satisfactory measurement of asphyxia and, secondly, a calculation of the degree to which a drug may be responsible for this asphyxia, when other factors may well have played a part in its production. Again, because of its rather indeterminate nature, no assessment was made, either subjective or objective, of the degree of analgesia obtained by the mother. In fact, there is every reason to assume that the analgesia obtained was completely adequate, since the primary benefit resulting from the use of nalorphine is that pethidine can be given to the labouring mother whenever she needs it. In particular, the use of nalorphine allows pethidine to be given during the most uncomfortable part of the first stage—namely, just before full dilatation. Its use late in the first stage obviates the rather unsatisfactory employment of the gas and air machine or trilene inhaler which are better left for the second stage.

In looking to the future use of nalorphine with pethidine, it is probable that the arbitrary amount of 10 mg. of nalorphine is capable of further refinement and should be adjusted in relation to the amount of pethidine estimated to be present in the foetal circulation. It is apparent that a time factor comes into this calculation as well as the total amount of pethidine that has been given. This correct adjustment is of double importance since nalorphine on its own, without pethidine, is also a respiratory depressant.

Finally, while there are obvious advantages to be obtained from the safe use of larger doses of pethidine, it is strongly felt that this is best reserved for institutional obstetrics, and indeed, those cases which need this range of dosage should, in any event, be delivered in hospital.

Acknowledgments

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THE ROLE OF THE OBSTETRICIAN IN MEGALOBLASTIC ANAEMIA OF PREGNANCY AND THE PUERPERIUM

BY

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MODERN obstetrical practice is based on the close collaboration of all who have an interest in the care of a mother and her child, the obstetrician having the closest and most direct contact with the patient. Physicians have been interested in megaloblastic anaemia of pregnancy since it was first described by Walter Channing in 1842 but over a century later Davis (1955), writing in a recently published, standard work on British Obstetrics, states that, "The features which distinguish it from other severe anaemias of pregnancy are not widely known". This represents a challenge to all practising obstetricians to make themselves more familiar with this condition. There have been many recent publications on this subject, but few by obstetricians, who undoubtedly have the greatest opportunity of detecting the disease in its early stages.

This paper is a summary of a clinical study of 52 patients suffering from megaloblastic anaemia of pregnancy or the puerperium, 35 being diagnosed and treated at the Princess Mary Maternity Hospital during the 8-year period 1948 to 1955, and the remaining 17 at the Newcastle General Hospital between January, 1955 and September, 1956. I personally saw 38 of these patients and Table I shows the apparent increased incidence of the condition in both hospitals from 1948 to the present time. Suggestions are made with the hope that they may help in detecting the disease at an earlier stage in pregnancy in view of the dangers to mother and child of severe anaemia being present at the onset of labour.

GENERAL FEATURES

The average age was 30·5 years with a proportion of multiparae to primiparae of 5 to 1. There had been a history of megaloblastic anaemia in a previous pregnancy in 3 instances and in 2 of severe anaemia requiring transfusion. From 25 dietary histories, 15 patients were considered to have an unsatisfactory intake of food, particularly of fresh meat and vegetables. Twins occurred in 5 instances, an unusually high incidence which was also the finding of Thompson and Ungley (1951).

CLINICAL FEATURES

The onset of symptoms was assessed as accurately as possible from the clinical history. In 46 patients it was between the 28th and 38th week; in 5 between the 20th and 24th weeks and in 1 in the early puerperium. An insidious onset

TABLE I
Number of Cases Treated 1948–1956

Year	1948	1949	1950	1951	1952	1953	1954	1955	1956	Total
Princess Mary Maternity Hospital	1	1	4	4	3	5	12	5	18	53
Newcastle General Hospital ..	2	3	3	2	3	2	6	5	12	38

occurred in 46 patients but in 6 it was acute accompanied by signs of congestive heart failure.

From an analysis of the main symptoms and signs the most frequently occurring features fall into 3 main symptom groups:

(1) *Those of anaemia:* pallor, listlessness, dyspnoea and frontal headache were common.

(2) *Those of gastro-intestinal upset:* anorexia and vomiting occurred in just under half of the patients with diarrhoea and sore tongue in a third of them.

(3) *Those of circulatory disturbance:* 37 patients had oedema, which was severe in 5; a haemic murmur was a common finding and 6 patients had an enlarged tender liver.

Pyrexia was common, occurring in 25 patients, 9 being ante-partum and 16 post-partum, the fever being unexplained in two-thirds of them.

Associated conditions were fairly numerous but few were of a serious nature. Pre-eclamptic toxaemia occurred in 11 patients, an incidence of 21 per cent.

The haematological findings showed a marked and wide variation, the only constant finding being a packed cell volume of less than 30 per cent and a mean corpuscular haemoglobin concentration of over 30 per cent. Blood films were not very helpful, megaloblasts being seen in only 5 instances. A bone marrow biopsy was taken in every case and all showed a megaloblastic erythropoiesis. This was considered essential for diagnosis, because of the frequency with which blood count values were equivocal.

Diagnosis

The time when the diagnosis was confirmed by marrow biopsy and treatment commenced is shown in Table II. From a careful study of the case records the reasons for admission to hospital or for the initial investigations were found to fall into 6 main groups, as follows:

(1) Six patients were specifically admitted for the investigation of anaemia of pregnancy or puerperium.

(2) Eight patients were admitted with pre-eclamptic toxaemia and were subsequently noted to have pallor.

(3) Eleven patients had puerperal pyrexia which did not respond to treatment with chemotherapy and antibiotics.

(4) Three patients had pyrexia of unknown origin.

(5) Four patients had an iron deficiency anaemia in the middle trimester of pregnancy, were successfully treated with iron and then relapsed in the last trimester or early puerperium.

(6) Twenty anaemic patients failed to respond to a period of regular iron therapy, either by mouth or injection.

For the above reasons a full blood count was performed and this, together with the clinical picture, gave rise to the suspicion that the anaemia was megaloblastic and a marrow biopsy obtained. The hospitals are fortunate in having a physician permanently available for consultation who saw nearly all of the cases, but the original clinical diagnosis and initiation of investigations were made by a member of the obstetric staff.

Table II
Diagnosis Confirmed by Marrow Biopsy

Ante-partum	32–36 Weeks	37–40 Weeks
29	14	15
Post-partum	**1–7 Days**	**7–14 Days**
23	17	6

Treatment

It has been fairly conclusively shown that in temperate climates the best response is obtained after treatment with folic acid and that treatment with vitamin B_{12} is ineffective (Thompson and Ungley, 1951; Scott, 1954). In sub-tropical and tropical zones good responses have been obtained with vitamin B_{12} (Chaudhuri, 1951), and it has been suggested by Adams (1956) that this is because there are several varieties of megaloblastic anaemia associated with pregnancy.

In this series good response to treatment was obtained with folic acid in 46 patients, with Citrovorum factor in 5 patients and with vitamin B_{12} in only 1 patient. Three patients initially treated with vitamin B_{12} failed to respond but subsequently improved with folic

TABLE III
Prenatal and Postnatal Diagnostic Incidence

Series	Number of Cases	Number Diagnosed Ante-partum	Number Diagnosed Post-partum
Stevenson (1938)	30	5	25
Davidson *et al.* (1942)	16	2	14
Thompson and Ungley (1951)	45	7	38
Clark (1952)	18	9	9
Scott (1954)	37	19	18
Lowenstein *et al.* (1955)	18	9	9
Present series (1956)	52	29	23

acid. Daily reticulocyte counts done from the first day of treatment showed a response in all cases varying from 2·5 per cent to 37·5 per cent, maximal on the 4th to 8th days of treatment. The response in puerperal patients was generally greater than those treated during pregnancy and they had a much more rapid increase in blood count values. In addition 36 patients received a blood transfusion of from 1 to 5 pints depending upon the severity of the anaemia. This was probably unnecessary in many instances but in 11 of the ante-partum cases it was given after the 37th week of pregnancy.

DISCUSSION

Until recent years this condition was mainly diagnosed in the out-patient clinic of the hospital physician, often weeks after the confinement. The women in many instances were critically ill and fatal results have been reported. In this series 29 cases were diagnosed before delivery and the remaining 23 in the immediate puerperium. Table III illustrates this increasing tendency for earlier diagnosis in reported series during the last 19 years. The insidious onset of this disease in the last trimester of pregnancy may easily be missed by the unwary examiner and should labour commence at this stage then the maternal prognosis becomes grave. There would appear to be a tendency for these anaemic women to start labour before term, Callender (1944) reporting 6 out of 25, Stevenson (1938) 8 out of 30 and in this series 18 women were delivered before the 38th week. Without early diagnosis there is no time to await the response to folic acid and blood transfusion is required, as was necessary in 11 of the patients.

Today, with improved antenatal care and the closer supervision of the pregnant patient, it should be possible for the obstetrician to detect those patients in whom the diagnosis seems likely. Suspicion may be aroused by a combination of pallor and gastro-intestinal symptoms, which occurred in 40 to 50 per cent of the patients, as they did in Callender's (1944) series. It is perhaps significant that only half of the patients were being investigated or treated for anaemia when the diagnosis was first suspected. As Miller and Studdert (1942) suggest, vomiting and oedema are frequently ascribed to pre-eclamptic toxaemia, a condition which is frequently associated and which occurred in 11 of the patients. Such patients were probably wrongly diagnosed as late toxic vomiting in former years. Pyrexia, another common finding, is often due to pyelitis or puerperal sepsis but if there is not a rapid response to treatment or the diagnosis cannot be confirmed bacteriologically then a full blood count is indicated. Many patients have an associated iron deficiency anaemia, Thompson and Ungley (1951) finding this particularly in untreated cases and in 5 of this series the anaemia responded initially to iron therapy only suddenly to relapse later in pregnancy, suggesting the need for careful follow up examinations. The most significant group contained anaemic patients who failed to respond to a period of regular iron therapy, in many cases given parenterally. This occurred in 20 patients and is also described in the series of Thompson and Ungley (1951), Israels and Da Cunha (1952) and Adams and Wilmot (1953). The pregnant patient with a refractory iron deficiency anaemia certainly warrants closer scrutiny.

The blood counts show such a wide variation that they are seldom very helpful, the more typical blood pictures occurring in the severe anaemias diagnosed in the late puerperium when the obstetrician is unlikely to see the patient.

Bone marrow biopsy readily establishes the correct diagnosis but this investigation should be interpreted with care for the rare case of haemolytic anaemia in pregnancy may elude the casual observer. The writer has seen such a case where macro-normoblasts, common in haemolytic anaemia, were mistaken for megaloblasts. Although both cells are abnormally large the megaloblast has an abnormal nucleus while that of the macro-normoblast, though large, has typical normoblastic characteristics. In such a case an initial reticulocyte count before commencing treatment would probably provide the clue to the correct diagnosis.

Megaloblastic anaemia, once thought to be a rarity is now a well recognized complication of pregnancy. Could it be that all pregnant women have a tendency to develop the condition and that a dietary deficiency or perhaps hormonal imbalance makes it manifest itself? In this connexion the high incidence of pre-eclamptic toxaemia in these cases is of interest and suggests a possible common factor. The aetiology of this condition is by no means fully understood and in the absence of a clear picture regular prenatal supplementary therapy as practised by Lowenstein, Pick and Phillpot (1955) has not found favour in this country. Once diagnosed, folic acid as a specific therapy will cure the illness but needs time to do it and the danger of premature labour occurring in patients near to term should not be overlooked for in these cases a preliminary blood transfusion is advisable.

Conclusion

Megaloblastic anaemia of pregnancy is now a well recognized disease which can be efficiently diagnosed and treated. If it is to be discovered before the patient becomes acutely ill with severe anaemia, then it is the obstetrician who is best able to detect the early signs. He should learn to suspect it in any pregnant woman showing signs of anaemia and as a means of early diagnosis the following suggestions are made:

(1) The haemoglobin should be checked routinely at the 34th to 36th week of pregnancy even though it was at a satisfactory level in earlier weeks.

(2) If the haemoglobin is below 70 (10 g.) per cent then a full blood count with haematocrit readings should be obtained. This is particularly desirable in the following instances.

(*a*) Anaemia associated with pre-eclamptic toxaemia.

(*b*) Anaemia associated with pyelitis of pregnancy.

(*c*) Anaemia associated with late toxic vomiting of pregnancy.

(*d*) An unexplained puerperal pyrexia or a puerperal infection not responding to treatment.

(*e*) Anaemia failing to respond to a period of regular iron therapy particularly if given parenterally.

(3) In interpreting blood counts a haemoglobin below 70 per cent with packed cell volume less than 30 per cent and mean corpuscular haemoglobin concentration above 30 per cent should be regarded as suspicious of a possible megaloblastic anaemia, remembering that post-haemorrhagic anaemia and anaemia secondary to sepsis can give similar readings.

(4) If the diagnosis of megaloblastic anaemia seems at all likely then a marrow biopsy should be performed without delay.

Summary

(1) The clinical features of 52 cases of megaloblastic anaemia of pregnancy and the puerperium are summarized.

(2) The onset of the disease was usually insidious, occurring between the 30th and 37th weeks of pregnancy.

(3) The common occurrence of other pregnancy complications with a very wide variation in the blood counts made diagnosis difficult and only one-half of the patients were primarily admitted for the investigation of anaemia.

(4) The difficulties of diagnosis are discussed, the importance of recognizing the early symptoms is stressed and suggestions of when to suspect the condition are made.

Acknowledgments

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AN EXPERIMENTAL STUDY OF THE EFFECT OF ISCHAEMIA OF THE PREGNANT UTERUS ON THE BLOOD PRESSURE*

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IN late toxaemias of pregnancy the first change is the development of systemic arteriolar capillary spasm. Finer methods of examination, for example microscopical study of the vessels of the conjunctiva or nail bed, examination of the retinal vessels, and of vaso-regulation by the cold pressor test or the pituitrin test, demonstrate the lability of the vascular system before toxaemic symptoms appear (Ivanov, 1952; Sauter, 1953; Landesman *et al.*, 1954). The most constant sign is the elevation of diastolic blood pressure, and the importance of the vascular changes is shown by the haemorrhages and necroses found in the liver and other organs after death from eclampsia.

In a previous report we have pointed out that the vascular changes are not satisfactorily explained on the basis of earlier theories (Gyöngyössy, 1956). We have discussed the theory of placental ischaemia as described by Page (1939), Beker (1948), Bastiaanse (1949) and Sauter (1953). According to this theory the late toxaemias are due to an insufficient blood supply to the gravid uterus, because of hypoplasia of the vascular system in primiparae, or because of increased intra-ovular pressure, or reduced hormone output. The hypoxaemic placenta emits impulses that induce systemic vasoconstriction, and the functional and organic changes in the various organs are the result of this.

Placental ischaemia might increase the blood pressure by two mechanisms. The majority of authors think that a humoral regulation is most likely (Page, 1948; Gorisontov, 1948; Reynolds, 1949; Bastiaanse and Mastboom, 1950; Assali *et al.*, 1952; Mastboom, 1952, 1953). It is possible that the ischaemic placenta produces a specific vaso-active agent. This might act directly on the blood vessels, or by increasing the production of vasopressin, renin or adrenaline, or by sensitizing the arteries to these hormones. It is also possible that hypoxia might impair the activity of the decidual detoxicating protective enzyme (Thompson, 1950; Fekete, 1952; Szontágh, 1953). In the maternal part of the placenta the activity of monoaminooxydase, which breaks down adrenaline and tyramine, and that of diaminooxydase, which breaks down histamine, would diminish. As a result the vaso-active amines from the foetal metabolism could reach the maternal blood unchecked. In the presence of hypoxia the decarboxylase function is increased, and histamine instead of histidine accumulates in the maternal blood and tyramine accumulates in the placenta (Page, 1948). In 1953 Mastboom also suggested that the enzymatic activity of the placenta is diminished, and that corticosteroid-like substances may be formed from the placental steroids instead of progesterone.

Alternatively it is possible that placental ischaemia may act through the nervous system. Receptors in the uterine wall and the nerve endings of the decidua might cause a reflex increase in blood pressure. This theory is supported by numerous morphological (Koppen, 1950; Szentágothai and Rajkovits, 1951), and

* This work has been supported by the Hungarian Medical Scientific Council.

clinical and experimental observations (Kekcheev and Sirovatko, 1938; Theobald, 1953; Lotis, 1953; Retchenko, 1954).

It is also possible that both humoral and nervous factors may be involved. In the present paper we wish to discuss the nature of the placental agent acting on the circulation, to describe its humoral transmission, and to discuss the possible nature of the agents involved.

Experimental Methods

Hypertension can be induced by clamping the aorta or the uterine arteries in gravid rabbits (Ogden, Hildebrand and Page, 1940) and dogs (Mastboom, 1949). Chesley and Alter (1951) have attempted to induce placental ischaemia by a *slow* perfusion of the living placenta in an oxygen-free medium. The aetiological role of uterine ischaemia has been demonstrated by uterine tonometry in cases of late toxaemia of pregnancy by Parviainen, Lankinen and Soiva (1951) and by Sauter (1953).

However, the hypertension after clamping the aorta in acute experiments may be explained as an alarm reaction, and the results obtained in the perfusion experiments are not convincing enough. We have not been able to develop a satisfactory method of carrying out chronic experiments, and so we too have induced uterine ischaemia in acute experiments by increasing the intra-ovular pressure. Three groups of experiments were performed.

In Group I dogs and cats near full-term were used. Laparotomy was performed under intravenous chloralose anaesthesia, and balloons were introduced into the amniotic sac of both gravid uterine horns. One balloon was attached to a water manometer and a Farkas syringe. The other balloon was used for recording uterine contractions, or it too could be used to distend the second horn. In some of the experiments the foetus was removed from the ovular cavity, but the placenta was left in place in every case. In most of the experiments the activity of the ileum was also recorded. The blood pressure in the carotid artery was measured with a mercury manometer (Fig. 1).

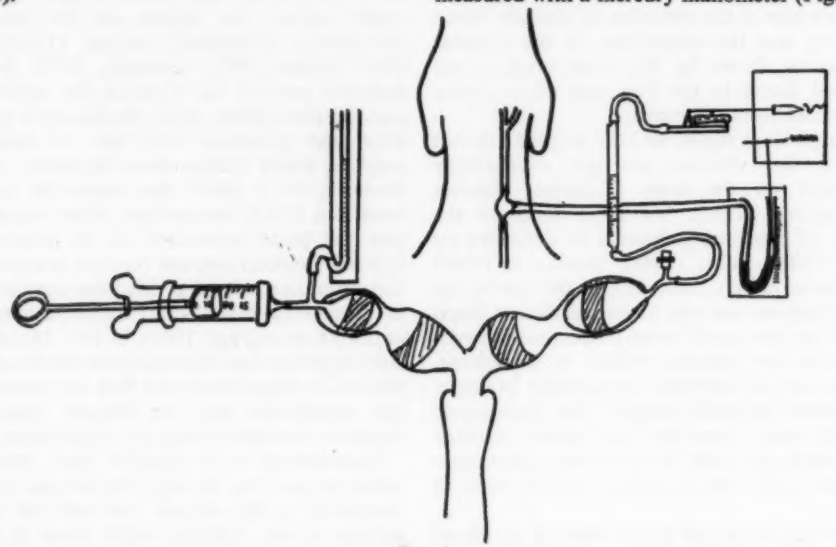

Fig. 1

Experimental arrangement. Induction of uterine ischaemia in dog and cat by increasing intra-ovular pressure. The balloons in the ovular cavity are filled up and pressure is measured by water manometer. Contralateral uterine horn activity and blood pressure are recorded kymographically.

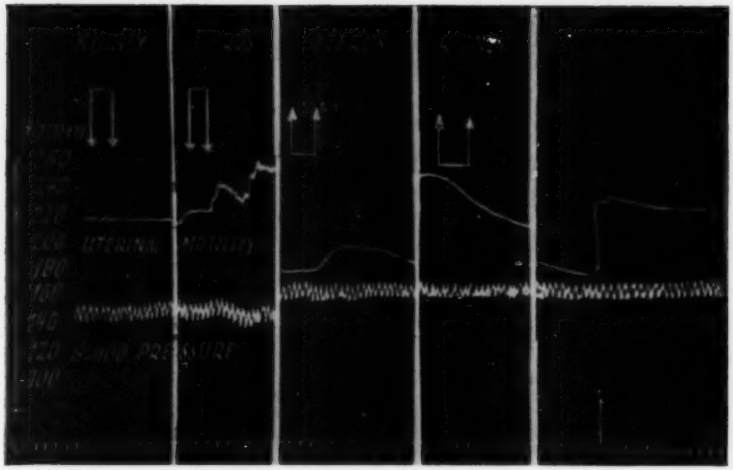

FIG. 2

Experiment 2. Gravid dog weighing 6·0 Kg. Six minutes after clamping the renal hilus pressure in the left uterine horn is adjusted to 200 ml. of water (section 2); 15 minutes later blood pressure is raised by 20 mm. Hg and remains at that level until 10 minutes after the release of the renal clamp (sections 3 and 4).

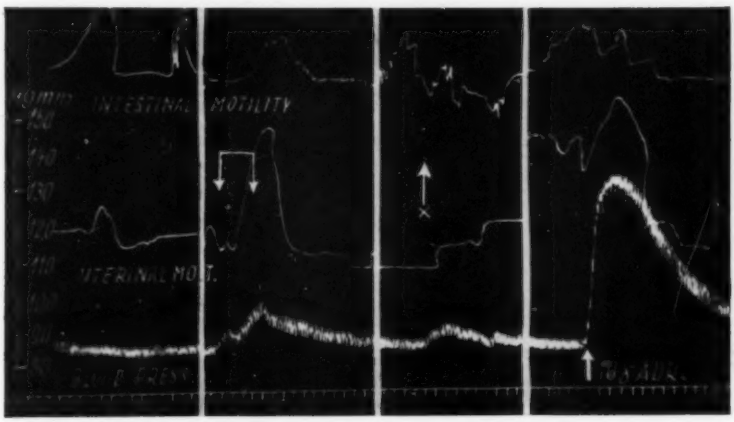

FIG. 3

Experiment 4. Pregnant cat weighing 2·4 Kg. On increasing pressure in the unilateral uterine horn blood pressure increases steeply by 40 mm. Hg (double arrow). The pressor effect lasts 10 minutes. The activity of the contralateral horn is increased (section 2). On allowing half the volume of fluid to flow out (x) blood pressure increases again by 20 mm. Hg and uterine tone increases. Ten gamma of adrenaline raises blood pressure by 130 mm. Hg and paralyzes uterine and intestinal functions.

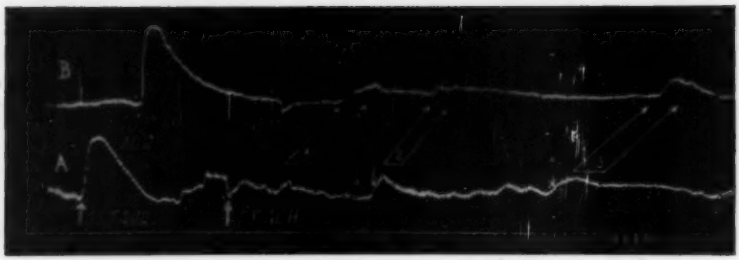

FIG. 5

Experiment 23. Gravid cat A (3·0 Kg.) and male cat, B (4·1 Kg.) Carotids connected. The pressor effect of adrenaline (ADR) is more marked in the male; the depressor effect of acetylcholine (ACH) is more marked in the gravid cat. On increasing intra-uterine pressure (double downward arrow) blood pressure rises steeply by 45 mm. Hg. On emptying the uterus (x) blood pressure slowly increases by 30 mm. Hg in cat A. Also, before increasing intra-uterine pressure the blood from cat A increases blood pressure by 20 mm. Hg in cat B. During the period of increased intra-uterine pressure blood pressure is elevated in cat B by 10 mm. Hg. The pressor effect after the cessation of uterine ischaemia amounts to 30 mm. Hg.

FIG. 6

Experiment 8. Non-gravid female cat weighing 3·5 Kg. One ml. of the concentrated perfusate from the gravid uterus of the dog elicits a biphasic blood pressure response: a 30 mm. Hg fall is followed first by a gradual, then by a steep rise of 90 mm. Hg. Intestinal peristalsis is paralyzed, then it is increased. The depressor effect does not develop when after 1 gamma histamine and 10 gamma adrenaline 1 ml. perfusate is given in combination with 5 mg./Kg. pyribenzamine. Peristalsis ceases, then increases. Ten mg./Kg. of pyribenzamine does not affect blood pressure.

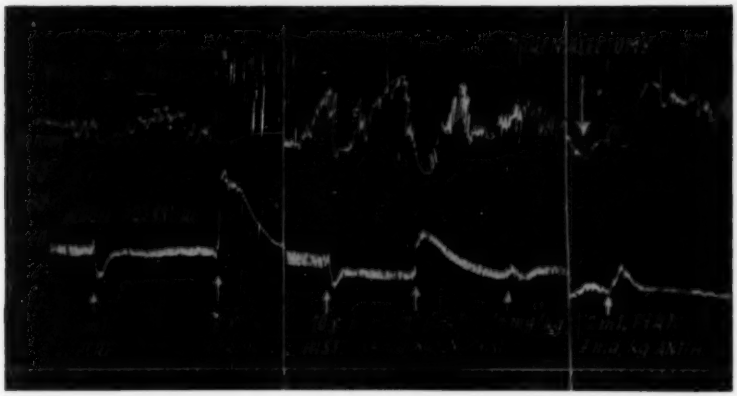

FIG. 7

Experiment 9. Non-gravid female cat weighing 1·7 Kg. The depressor effect of 4 ml. perfusate from the gravid uterus of the cat is comparable to that of about 10 gamma histamine. The effect is reversed when perfusate is injected together with an anti-histaminic. Peristalsis ceases, then increases.

After the blood pressure had reached a stable level the intra-ovular pressure was adjusted to 60 or 120 mm. of water, on one or both sides, by injecting water at body temperature. The increased pressure was maintained for 8 to 20 minutes in the dogs, and for 5 to 10 minutes in the cats. Some of the experiments were also combined with the application of a clamp to the renal hilum, with adrenalectomy, and with the administration of ergotamine and atropine. In control experiments we used normal animals, or animals on the first or second day of the puerperium.

The experiments were also repeated in women in whom pregnancy had to be interrupted for various reasons either vaginally or abdominally. At laparotomy performed under Evipan anaesthesia the uterus was distended with Locke's solution through a needle inserted into the ovular cavity. At the vaginal operations 20 per cent dextrose was introduced through a catheter. In both cases the blood pressure was recorded at intervals of 2 to 5 minutes.

In Group II parallel blood pressure experiments were made on gravid cat A and male cat B. In one case blood from cat A was transferred to cat B with a syringe. In the other experiments the central carotid stump of A was connected with the peripheral carotid stump of B by a "Telcothene" sleeving tube. Blood was transferred before, during and after the induction of uterine ischaemia in cat A.

In Group III perfusates were prepared from the uteri of gravid animals. The ovarian arteries and veins were ligatured, the uterine cavity was filled, and the uterine vessels were then washed through *in situ* with Locke's solution. The perfusates were concentrated to one-tenth of the original volume and were then studied in combination with antihistamines, etc., or adrenalectomy, to determine the effect on the blood pressure when injected into dogs and cats.

Ten dogs (6 gravid, 2 puerperal, 2 normal females) and 24 cats (11 pregnant, 4 puerperal, 9 males or normal females) were used in the experiments.

Results

(1) *Pressor Effect of Uterine Ischaemia*

Ischaemia of the gravid uterus was induced on 9 occasions in 6 dogs by increasing the intra-ovular pressure for 7 to 20 minutes (Table I). A slow increase of blood pressure was noted, which continued to increase after the uterine filling had ceased, and which did not return to the initial level until 10 to 20 minutes later. As it develops very slowly the pressor effect is rather difficult to distinguish from the physiological variations in blood pressure. In two animals the filling of the pregnant uterus was combined with clamping the renal hilum (Fig. 2). Renal ischaemia had no synergistic pressor effect. In the control experiments on puerperal and normal female dogs increasing the intra-ovular pressure did not raise the blood pressure; on the contrary, in the case of a normal uterus, a transient fall of 25 mm. Hg occurred, and this observation is in agreement with that of Mastboom (1949).

TABLE I

Changes in the Blood Pressure on Filling Up the Uterine Cavity of the Dog

Designation	Change in Blood Pressure (mm. Hg)	Duration of Filling (minutes)
No. 1: gravid	+30	7
	+30	10
No. 2: gravid	+25	15
	+20	15
No. 3: gravid	+20	20
No. 5: gravid	+25	10
No. 13: gravid	+40	10
	+10	20
No. 16: gravid	+20	20
No. 29: puerperal ..	+5	10
No. 30: puerperal ..	−10	7
No. 10: normal ..	−25	5
	±0	8

Eighteen experiments have been made on 11 pregnant cats (Table II). Biphasic blood pressure responses were obtained. The increase of intra-uterine pressure was followed by a rapid rise of blood pressure of 15 to 65 mm. Hg, and this was followed by a second prolonged rise after the intra-uterine pressure had been released. The second rise was up to 30 mm. Hg (Fig. 3). The blood pressure responses tended to become smaller and smaller on repetition of the filling and evacuation of the uterus. This tachyphylactic phenomenon is also seen in carrying

TABLE II

Changes in the Blood Pressure on Filling Up and Emptying of the Uterine Cavity of the Cat

Designation	Change in Blood Pressure on Filling Up (mm. Hg)	Emptying (mm. Hg)	Duration of Filling Up (minutes)
No. 4: gravid ..	+40	+20	10
No. 7: gravid ..	+35	+15	8
No. 11: gravid ..	+65	+10	10
	+30	±0	4
	+20	±0	5
No. 14: gravid ..	+30	±0	13
	+30	+10	10
	+20	+20	13
No. 15: gravid ..	?	+30	30
No. 19: gravid ..	+30	±0	7
	+10	±0	15
No. 20: gravid ..	+45	+25	10
No. 21: gravid ..	±0	+30	5
	+10	?	8
No. 23: gravid ..	+45	+30	8
	+20	?	7
No. 24: gravid ..	+15	+25	7
No. 28: gravid ..	+15	±0	8
No. 22: puerperal ..	+5	±0	8
	±0	±0	10
No. 25: puerperal ..	+5	±0	8
	+5	±0	7
No. 26: puerperal ..	+5	+7	8
No. 27: puerperal ..	+5	±0	10
	±0	±0	6
	±0	±0	6
No. 12: normal ..	±0	±0	5
	±0	±0	10

out the toxicotest* of Péteri and Tarján (1950).

The contralateral horn of the uterus responds to the filling and decompression by increased activity. The investigations of Surányi, Kovács and Molnár (1955) showed that this was due to a spinal reflex. Changes also occurred in intestinal motility, but with less constancy. In some cases intestinal activity ceased on increasing the intra-uterine pressure, whereas on releasing the pressure mass contractions occurred.

Ten experiments were made on the uteri of 5 puerperal and normal cats. Uterine ischaemia had no substantial influence on the blood pressure. Increases observed, ranging from 5 to 7 mm. Hg, were within the limits of physiological variation. On release of the intra-uterine pressure an increase in intestinal activity was also observed in these animals.

The experiments were repeated in 4 human subjects (Fig. 4). In Case 1 hysterotomy and sterilization were performed at the fourth month

* Toxicotest. Péteri and Tarján (1950) have observed that serum from a toxaemic patient causes a fall in the blood pressure of the cat similar to that produced by histamine, whereas serum from normal pregnant subjects has no effect on the cat's blood pressure. This observation is the basis for a diagnostic test ("toxicotest") for the early detection of toxaemia.

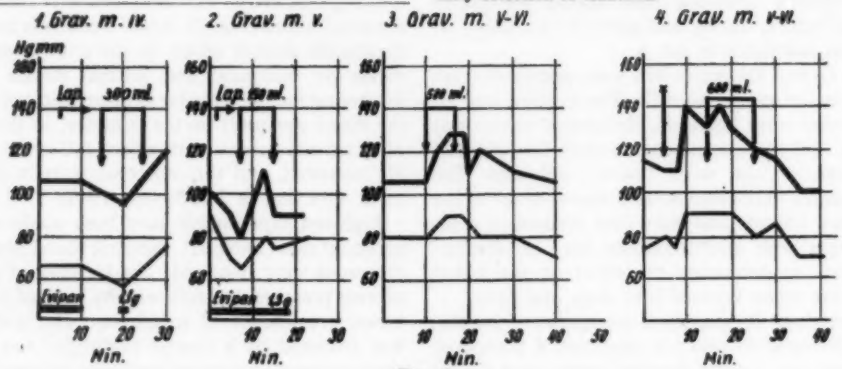

FIG. 4

Human pregnancy

Blood pressure response to the increase in the intra-ovular pressure of the gravid uterus:

1 and 2: Evipan anaesthesia. Laparotomy. Introduction of Locke's solution into ovular cavity through needle.

3 and 4: Introduction of 20 per cent dextrose through intra-ovular catheter.

x: Cervix is pulled down.

because of imbecility. In Case 2 hysterectomy was performed in the fifth month for carcinoma of the cervix. Intra-ovular filling of the uterus increased the blood pressure by 25 to 30 mm. Hg, even while the patient was under the effect of intravenous anaesthesia. In Case 3 vaginal termination was performed in the fifth month because of pyonephrosis, and Case 4 was also terminated vaginally for heart failure in the sixth month. In the unanaesthetized patient distension of the uterus raised the blood pressure by 20 to 30 mm. Hg for 20 to 25 minutes. In Case 4, however, the blood pressure increased when the cervix was drawn down, before the uterus was filled; this confirms the observations of Kekcheev and Sirovatko (1938) and Theobald (1953) that mechano-receptors exist in the cervix.

(2) *Parabiosis Experiments*

In one instance blood taken from gravid cat A before, during and after increasing the intra-ovular pressure was injected into male cat B (Table III, number 20). A remarkable reversal of effect was seen. The blood obtained before increasing the intra-uterine pressure reduced the blood pressure of cat B by 15 mm. Hg. The blood obtained while the intra-uterine pressure was raised had no effect on the blood pressure, while the blood drawn after the pressure was released increased the blood pressure by 25 mm. Hg.

In 3 experiments the circulations were connected by way of the carotid vessels. On allowing blood to flow from one animal into the other before increasing the intra-uterine pressure, in one case the blood pressure in cat B did not change (No. 24), whereas in two other cases the blood pressure in cat B rose by 7 mm. and 20 mm. This appears to contradict the statement that the intravenous injection of homologous blood will lower the blood pressure in the cat. It is possible that in these two cases anaesthesia and the manipulations caused a degree of uterine ischaemia.

On allowing blood to flow into animal B during and after the induction of uterine ischaemia in animal A, the pressor effect developed in all three cases, to some degree during, but to a greater degree after, the uterine ischaemia. In animal A the rapid "filling" and milder "release" effects took place, as described above.

(3) *Experiments Using Perfusate*

The next step was to investigate the substances involved in the humoral mechanism. We have already mentioned the experiments that were combined with clamping the renal hilum. In other experiments on cats adrenalectomy did not inhibit but only lessened the pressor effect of uterine ischaemia. In contrast to this, after treatment with ergotamine (gynergen) the increase in blood pressure did not occur. Likewise the "Umkehr" effect characteristic of adrenaline failed to develop.

The effect of uterine perfusates on the blood pressure was tested in 3 experiments on dogs

TABLE III

Changes in the Blood Pressure of Gravid Cat "A" and Male Cat "B" in Parabiosis, on Filling Up the Gravid Uterus

Designation	Blood Pressure of "A"		Blood Pressure of "B" on Injection of Blood from "A"		
	On Filling (mm. Hg)	On Emptying (mm. Hg)	Prior to Filling (mm. Hg)	During Filling (mm. Hg)	During or After Emptying (mm. Hg)
No. 20*	+45	+25	−15	±0	+25
No. 23	+45	+30	+20	+10	+30
No. 2	+15	+25	±0	+20	+25
No. 28	+15	±0	+7	+7	+15

* Transfer of blood by syringe.

and 4 on cats. Intravenous injection of the perfusate of the uterus of the gravid dog into the same animal resulted in a prolonged elevation of the blood pressure. The same was seen in male dogs, but in them the effect hardly exceeded the range of physiological variation. Uterine perfusate of the non-pregnant dog has no effect on the blood pressure when it is injected into the same animal; the sole response was the appearance of strong intestinal contractions reminiscent of an acetylcholine effect. This is in agreement with Mischel (1954), who showed that the non-pregnant uterus contains large amounts of acetylcholine.

The concentrated perfusate of the uterus of the gravid dog elicits a biphasic blood pressure response in the cat. An initial fall in pressure is followed by a slow then by a rapid rise. Intestinal motility ceases. The blood pressure falls later, but even after 8 to 10 minutes it is above the initial level. The first fall in blood pressure is comparable to that produced by 2 gamma histamine, and the increase is similar to that produced by 5 to 6 gamma adrenaline. When the perfusate is administered in combination with an antihistamine the first fall does not occur, and only the rise is observed. This is not due to a pyribenzamine effect, as the blood pressure does not increase when the dose of antihistamine is doubled and it is given alone (Fig. 6).

The perfusate of the uterus of the gravid cat causes a similar biphasic effect in the male cat, but the initial fall is more marked, and the subsequent rise less steep. On the combined administration of perfusate and antihistamine only the pressor effect was seen. The perfusate of the uterus of a cat at mid-pregnancy induced in the male cat only a fall in blood pressure, which was comparable in degree to that produced by 10 gamma histamine (Fig. 7). The blood pressure became established at a level not lower, but higher than the initial pressure. The effect is reversed when the perfusate is given in combination with antihistamine; intestinal motility ceases, then strong peristalsis develops, reminiscent of an acetylcholine effect. The antihistaminic alone has no pressor effect. Adrenalectomy does not prevent the development of the pressor effect of perfusate of the ischaemized pregnant uterus.

Discussion

The experiments described show that ischaemia of the gravid uterus elicits a pressor response in the cat and in woman, and less convincingly in the dog. In the cat the cessation of ischaemia is followed by a second more protracted increase in blood pressure. The pressor effect appears to be related to the placenta, as it can be elicited in the absence of the foetus, but not in the puerperal animal in which there is no placenta.

At least in part the pressor effect depends upon a humoral mechanism. The immediate and rapid rise of blood pressure that occurs when the intra-ovular pressure is raised is probably partly due to a nervous reflex mechanism, but the second milder increase of blood pressure seen in the cat when the uterine ischaemia ceases seems to be humoral in nature. The blood pressure of a second animal in parabiosis shows the same elevation when the intra-uterine pressure is released.

The perfusion experiments showed that vaso-active substances can enter the circulation from the placenta. Histamine, or some histamine-like substance must be among them, as anti-histamines prevent or reverse the depressor effect. This view is supported by the observation that histamine concentration is increased in the serum and cerebrospinal fluid of women with toxaemia of pregnancy. An acetylcholine-like substance may also be involved in the depressor effect, as is suggested by the appearance of increased intestinal peristalsis after the administration of perfusate from the gravid uterus, or after the cessation of uterine ischaemia. On the administration of atropine these intestinal contractions ceased, and if the blood pressure had returned to normal (after the rise that followed the release of the intra-uterine pressure) a further rise of blood pressure was seen. However, perfusates from non-pregnant and puerperal uteri also increased intestinal activity, so that this effect is not of placental origin. All that may be suggested is that the uterus containing the placenta may supply more choline-like substance to the circulation. It is possible that acetylcholine is an agent that not only initiates labour and serves as a methyldonator, as Mischel (1954) has suggested, but that it is also a factor in regulating blood pressure.

With regard to adrenaline our results are equivocal. A pressor effect, but of less degree, developed after adrenalectomy both on inducing uterine ischaemia and on the injection of perfusate. Ergotamine abolished the pressor effect, but the inverse effect characteristic of adrenaline did not appear. On the other hand, in a few cases uterine ischaemia caused an intestinal inhibition similar to that caused by adrenaline. Moreover, uterine ischaemia changed the sensitivity of the animal to adrenaline. This seems to indicate the involvement of adrenaline or noradrenaline in the pressor effect. It is possible that the ischaemic placenta releases an adrenaline-like substance, or an agent which mobilizes the adrenaline or noradrenaline of the pregnant organism. It might also be suggested that anoxia would reduce the activity of placental monoaminooxydase, and that monoamines which have a pressor effect would then accumulate.

It is also conceivable that pressor agents are produced as a counter-response to the depressor agents histamine and choline. Went, Szücs and Kovács (1954) have called attention to this possibility. They found that acetylcholine and histamine induced the production of antagonistic adrenergic mediators.

The experiment in which we clamped the renal hilum showed that renal pressor agents were not responsible for the effect. This view is supported by the experiments of Gorontisov (1948) and Kogan (1951), in which it was not found possible to induce renal hypertension in gravid animals, because the angiotonic effect of renal ischaemia was neutralized during pregnancy. On the other hand Franklin (1954) has put forward the view that utero-renal factors cause hypertension in pregnancy.

Our experiments suggest that the blood pressure in pregnancy is affected by both neural and hormonal factors. On the one hand the increased tension in the uterine wall, or substances produced in the ischaemic uterus which may stimulate nerve endings in the decidua, may increase the blood pressure by a viscero-sensory reflex. On the other hand these agents may enter the circulation and cause hypertension in the suceptible nervous and vascular system of the pregnant woman.

Summary

The theory that late toxaemia of pregnancy is due to utero-placental ischaemia is reviewed. It is not certain whether hypertension is caused by a humoral or a nervous mechanism.

The authors induced placental ischaemia by distension of the gravid uterus. Humoral transmission of the pressor effect has been studied in parabiosis experiments in cats. The pressor effect of perfusate from the ischaemic gravid uterus has been studied in cats.

By increasing the intra-uterine pressure the blood pressure can be raised in the gravid cat, dog and woman. The pressor agent is derived from the placenta, and can be transferred humorally into another animal. In the cat the release of intra-uterine pressure is followed by a second pressor response, which is more prolonged but of less degree, and can be transferred humorally into another animal. Apparently the pressor effect begins with a viscero-sensory reflex, but humoral factors are responsible for the prolongation of the effect. One of the placental vaso-active agents is a histamine-like substance, but a choline-like agent may also be involved. Simultaneous renal ischaemia or adrenalectomy has no effect on the pressor mechanism.

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THE ACCURACY OF RADIOLOGICAL ESTIMATION OF FOETAL MATURITY

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INTRODUCTION

IT has been stated (Roberts, 1935; Hodges, 1937) that a radiologist of experience can usually give a reliable estimate of foetal maturity by simple inspection of X-ray films, basing his assessment on the size of the foetus and the stage of ossification of its bones. For some time, one of us (F.R.B.) has been estimating foetal maturity in this way but, lately, we have been wondering whether this method is accurate. We decided, therefore, to review our own results in a series of 200 unselected cases, and to find out whether a study of wrong estimates would throw light on possible sources of error.

MATERIAL

A consecutive series of pregnancy films was collected. Films were discarded if the foetus was dead at the time of radiography, or if there was any doubt about the date of the last menstrual period, the duration of menstrual cycles or the duration of pregnancy at the time when the films were taken. Therefore the series does not contain any case in which the films were taken for the purpose of estimating maturity, except where the dates were absolutely certain but seemed to conflict with the physical signs (e.g., size of foetus). Eventually a total of 200 cases remained in which radiography had been carried out at the request of clinicians for various other reasons.

THE METHOD OF INVESTIGATION

The case histories were checked by the clinician (B.E.) and the maturity of the foetus on the day of radiography was calculated, to the nearest week, from the menstrual history. The radiologist (F.R.B.) estimated the maturity to the nearest week on the films submitted after delivery, but he was not given any clinical information. This assessment in retrospect precluded the taking of any additional films if those available were regarded as unsatisfactory. However, no extra radiation was given to any patient as a result of this investigation. In this series no attempt was made to estimate postmaturity; the most advanced estimates were given as "at term".

After the maturity estimates had been made in 200 cases, they were reviewed jointly by the clinician and the radiologist. The clinical features of the cases were considered, and, in an attempt to find the causes of these errors, the films were re-examined in all cases where the estimate was incorrect by two or more weeks.

RADIOGRAPHIC TECHNIQUE

The standard technique (carried out with the patient lying) was to take 2 films, one anteroposterior and the other lateral, the whole of the foetus being shown on each film. Abdominal compression was used according to the method of Hartley (1954) without the use of a wedge filter for the lateral films. Some of the cases in this survey had had films taken for pelvimetry and the lateral films of these patients were exposed with the subject standing and were centred over the pelvis, so that the whole of the foetus was not included on the film. For some other cases, placentography had been carried out, which resulted in the addition of an erect

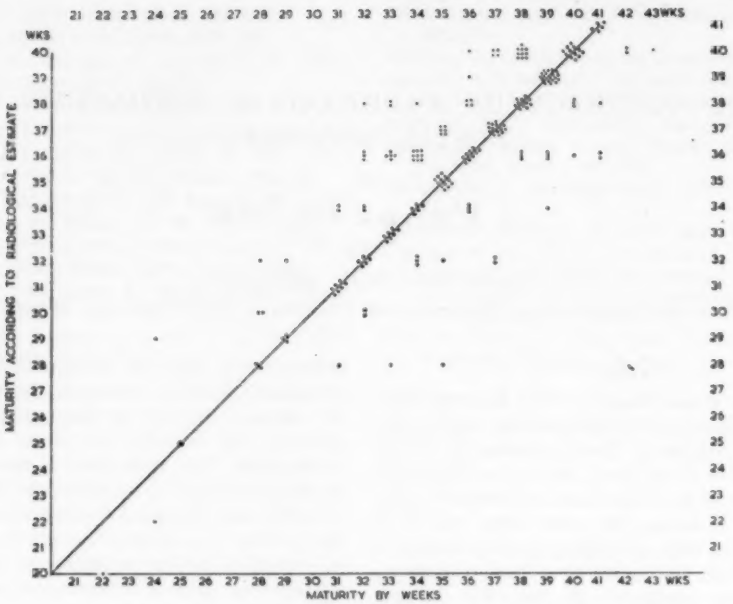
MATURITY ACCORDING TO RADIOLOGICAL ESTIMATE
WKS
MATURITY BY WEEKS
21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 WKS

FIG. 1

Radiological estimate of maturity in 200 cases compared with maturity by dates. (The 112 cases recorded on the diagonal line are those in which the estimates agreed completely or differed by not more than 1 week; 32 were under-estimated, and 56 were over-estimated.)

lateral film, and on occasions, another lateral film with the patient leaning backwards. Again, on these 2 special lateral films the whole of the foetus was not included. Moreover, a postero-anterior film was substituted for the usual antero-posterior film and the effect of this was to reduce the apparent size of the foetus because, being nearer to the film, it was not enlarged as much as it would have been on an antero-posterior film. It will be seen, therefore, that the pelvimetry films did not give as much information on the size and structure of the foetus as the standard technique, but that was not so in the placentography examinations.

OBSERVATIONS

(1) RESULTS

In Figure 1 radiological estimates of maturity of 200 pregnancies are recorded individually. The cases placed along the diagonal line are those in which there was complete agreement between the radiological and clinical estimations and also those in which they differed by 1 week. Because the calculated foetal maturities were taken to the nearest week it follows that the radiological estimates of the cases recorded on the line could have differed by as much as 10 days from the real foetal maturities. It will be noted that, of the cases where the radiological assessment was wrong, more maturities were over-estimated (28 per cent, i.e., 56 cases above the diagonal line) than were under-estimated (16 per cent, i.e., 32 cases). Duration of pregnancy at the time of radiography ranged from 23 to 43 weeks.

The aggregate results in terms of accuracy of radiological estimates are shown in Figure 2. In 112 cases (56 per cent) the estimate was correct to within 1 week or less on either side

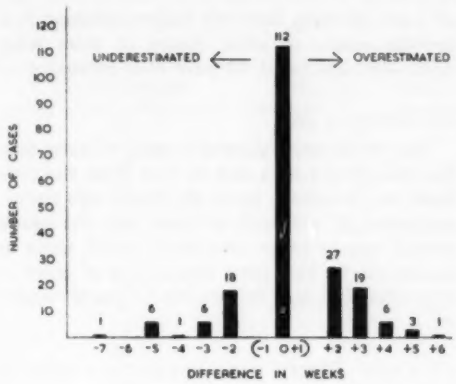

FIG. 2

The frequency distribution among 200 foetuses of the difference between the maturity estimated radiologically and the maturity by dates.

of the calculated maturity. The histogram shows that the number of cases decreased with the severity of the error, as one would expect. In 157 cases (78·5 per cent) the estimate came within 2 weeks of the known maturity.

Although the spread from the diagonal line in Figure 1 is about the same at all stages of foetal maturity, a higher proportion of the more mature foetuses are recorded on the line, showing that the greater the maturity the more accurate was the method. The radiological estimates were mostly given to the nearest "even" week because it was usually impossible to make a more accurate assessment of foetal development. Therefore, nearly all these cases appearing on the diagonal line in odd weeks had in fact been assessed radiologically to the nearest "even" week above or below the line. For the same reason, cases where the radiological estimate was 40 weeks and the real maturity 41 weeks are placed on the diagonal line at 41 weeks.

(2) Possible Sources of Errors of Estimated Maturity

Re-examination of the films of 88 incorrect estimates was carried out with special reference to the quality and number of the films, presentation, sex of foetus, number of foetuses, weight of the child when born and height and weight of the mother.

(a) *Number and Type of Films Used*

Amongst 79 errors from the 32nd week onwards the available films were unsatisfactory for maturity estimates (e.g., relevant parts of the foetal skeleton not clearly demonstrated) in 18 cases, i.e., 23 per cent.

Errors were made 16 times (20 per cent) when pelvimetry films (total 45) were used. The maturity was over-estimated in 7 cases and under-estimated in 9 cases. The proportion of errors to total pelvimetry examinations (16 to 45) does not differ significantly from that of the whole series (88 to 200). Out of the series of 10 placentographies, the estimate was incorrect in 3, which again is no greater than in the whole series.

(b) *Ossification Centres*

The presence of centres in the knee at 32 weeks led to over-estimated maturity in 4 cases, in 3 of which there were 4 centres (2 lower femoral and 2 upper tibial epiphyses). There was 1 error at 33 weeks and 2 at 34 weeks; they all showed the 4 centres. From the 36th week onwards the number of erroneous estimates with 4 centres increased, as one would expect. On the other hand, there was 1 erroneous estimate at 39 weeks where no centre was present, similarly 1 at 38 weeks and 2 at 37 weeks. It would seem that the presence or absence of centres may be equally misleading.

(c) *Size of Child*

In the 200 patients the child was comparatively small at birth in 26. These children were 2,750 g. in weight or less if born at 40 weeks or correspondingly lighter if born earlier. The radiological estimate was correct within 1 week in 14 of these. Its maturity was under-estimated 10 times but it was over-estimated only twice.

Children weighing 4,050 g. or more at 40 weeks or correspondingly heavier than the normal if born earlier, were classified as large children. There were 24 such children. Their maturity was estimated correctly in 15 cases.

It was over-estimated 9 times but it was never under-estimated.

Thus as one would expect, there was a tendency to under-estimate if the child was small and to over-estimate if it was large.

(d) *Small Stature of the Mother*

If the mother was of small stature (5 feet or less) the estimate was not influenced significantly (over-estimated 5; under-estimated 4).

(e) *Weight of the Mother*

Where the mother was above average weight (over 82 Kg.) the maturity was over-estimated in 6 cases and under-estimated in 3.

In mothers below average weight (under 59 Kg.) 2 maturities were over-estimated and 4 were under-estimated.

Thus, if the mother was heavy, there was a tendency for foetal maturity to be over-estimated, the opposite being observed in slight women.

(f) *Sex of Foetus*

Excluding 1 abortion, there were 94 foetuses amongst 88 erroneous estimates (6 sets of twins). Forty-two were females and 52 were males. Allowing for the greater number of male births in the general population, the difference is not sufficient for us to conclude that the sex of the child predisposed to errors in the estimates. This is also shown in the ratios of over- to under-estimated maturities in the 2 sexes:

Males:	32 (over) : 20 (under)	=1·6
Females:	26 (over) : 16 (under)	=1·6

(g) *Twins*

Out of 14 sets of twins, an erroneous estimate was made in 6. Four were over-estimated and 2 were under-estimated. This may seem rather surprising, but a radiologist would always be on his guard against under-estimating the maturity of twins because of their small size and, therefore, in this series had presumably over-corrected his impression.

(h) *Breech*

In 17 out of the 29 breech presentations (twins excluded) the estimate was inaccurate by 2 weeks or more showing that this malpresentation is a definite source of error. Seven of these were under-estimated and 10 were over-estimated.

(i) *Transverse Lie*

The whole series showed 9 cases of transverse lie (excluding twins) and in 5 of these the estimate was incorrect. In all the foetus was under-estimated. It is difficult to know why the foetus should appear to be abnormally small when in transverse lie but, once this source of error is appreciated, it may be possible to guard against it.

(3) Cases Where the Inaccuracy was 4 Weeks or More

The following were the main causes for gross errors: unsatisfactory films (2 cases), the absence of centres of ossification at the knee after 36 weeks (3 cases), the presence of 4 centres at the knee before 36 weeks (5 cases), abnormal size of foetus (4 cases), transverse lie (2 cases) and twins (1 case). In some radiographs in the series, two of these causes of error were noticed. It would appear that the period between the 28th and 33rd week is an exceptionally difficult one for the estimation of maturity (see Table I).

Discussion

The results in this series indicate that the value of radiological estimation of maturity has the following limitations. With films taken mainly for purposes other than determination of maturity, an estimate accurate to within 1 week can be expected in 56 per cent of cases; in 78·5 per cent of cases the estimate comes within 2 weeks of the correct maturity. The radiologist cannot give an absolute guidance. As Williams (1950) has pointed out, the radiological estimate can only be approximate and must be considered by the clinician together with all the other clinical data. With a large child the maturity may be over-estimated; it may be under-estimated if the child is small. We cannot, given a film, be certain whether a possible coefficient for correction should be applied. Indeed, the problem is not of an academic nature as to whether the radiological estimate is more often right or wrong. In obstetric practice

TABLE I

Errors of 4 Weeks or More

Clinical Estimate	Radiologist's Estimate	Comment
37	32	No centre at the knee, 2,400 g.
37	32	No centres at the knees, 2,100 g. at 45 weeks.
39	34	No centres at knee. Transverse lie.
41	36	Unsatisfactory films for showing knee centres.
40	36	Unsatisfactory films.
34	38	4 centres at the knee.
35	28	Transverse lie.
34	38	4 centres at the knee.
35	28	Transverse lie.
34	38	4 centres at the knee.
24	29	Only 1 film available.
28	32	Twins, 2,375 g. and 2,450 g. at 34 weeks.
32	36	4 centres at the knee.
32	38	4 centres at the knee, 4,500 g. at 41 weeks.
32	36	4 centres at the knee.
32	36	2 centres at the knee.
33	28	—
33	28	—
33	38	2 centres at the knee.
41	36	—

one is typically faced with a patient whose expected date of delivery is unknown or uncertain, or the case of the foetus which seems smaller or larger than average for the duration of amenorrhoea.

Our results could probably have been improved by the use of X-ray films taken for the specific purpose of determining foetal maturity. We agree with Hartley (1957) that with high quality films a greater degree of accuracy should be obtainable. Hartley (1957) claims that there is a fairly constant pattern of foetal skeletal development and, provided high quality films are obtained, a high degree of accuracy can be achieved in estimating foetal maturity radiologically. He emphasizes that the lower epiphyseal centre of the femur begins to appear at 36 weeks and the upper epiphysis of the tibia at 38 weeks. We have been misled repeatedly by the presence of both centres in both lower limbs as early as 32 weeks. We also noticed the absence of these centres as late as 39 weeks.

Many attempts have been made to measure parts of the foetal skeleton or to determine the developmental stage of the skeleton by X-rays without introducing a personal factor. It is improbable that the method of estimating maturity used in this series is less accurate than other methods which exclude the personal element but are based on measurement of some part of the foetus, e.g., the bi-parietal diameter. Ince (1939), measuring this diameter at birth and on the fourth day of life in order to allow for moulding to subside, as well as in children delivered by Caesarean section, found that it ranged from 3·30 to 4·05 inches at term, so that even estimation of maturity based on it will not be accurate. These measurements corresponded to a weight range between 1,650 g. and 4,250 g. Thus for a bi-parietal diameter of 3·85 inches the weight varied between 2,650 g. and 5,125 g. with an average of 3,550 g. This range of 2,500 g. makes the method useless also as a means of estimating the size of a given foetus. According to Roberts (1935), it would be unreasonable to expect all foetuses to have bi-parietal diameters of standard size when delivered as the weight of the foetus at term may range from 1,850 g. to 4,100 g. "The variation in weight is found to be out of all proportion to the variation in cephalic measurements." Hodges (1937) determined the foetal age from dimensions of skull and extremities. Although he acknowledged inescapable variations in foetal size and age, he

was of the opinion "that in suitable cases, careful roentgen estimates of foetal age may be more dependable than the menstrual history".

Summary and Conclusions

Radiological estimation of foetal maturity was carried out in retrospect in a series of 200 women in whom there was no doubt about the duration of pregnancy. The method consisted in simple inspection of X-ray films.

A study of the cases in which an erroneous estimate had been made led to the following conclusions:

(1) If, with the recent trend to reduce radiography in pregnancy, films of poor quality or those taken for other purposes are utilized for estimating maturity, errors are more likely to be incurred.

(2) If the foetus is above average size, its maturity is liable to be over-estimated and vice versa in the case of small foetuses.

(3) Malpresentation was a definite source of error, but not the sex of the foetus. Correct estimation of maturity was comparatively difficult between the 28th and 33rd week of gestation.

(4) Maternal height did not influence the radiological estimate. If the mother's weight was above average, there was a tendency to over-estimate foetal maturity. The reverse was observed in slight women.

(5) With good quality films the method of simple inspection probably does not lead to more errors than estimates based on measuring certain parts of the foetal skeleton.

(6) It would therefore seem unwise to disregard clinical features and base the management of a given case mainly on radiological estimation of foetal maturity, particularly if X-ray films are not of high quality.

Acknowledgment

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THE ARTIFICIAL KIDNEY AND THE TREATMENT OF ACUTE RENAL FAILURE*

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THE DIETARY REGIME IN ANURIA

BORST (1948) and Bull, Joekes and Lowe (1949) stressed the importance of fluids and dietary restriction in the treatment of anuria. Bull *et al.* (1949) used 100 g. of peanut oil, 400 g. glucose and water to one litre. In this mixture approximately one litre of fluid was given to balance the insensible loss of water during the anuric period, and the glucose and fat were given to suppress protein metabolism, thereby delaying the onset of the uraemia. Today this dietary regime, as we have termed it, is still the basis of modern therapy but the ingredients and the quantities have been altered to satisfy more recent knowledge.

First let us consider the fluid requirements. In patients with anuria approximately 400 to 600 ml. of water are released in the course of metabolism. Some of this water is an end product of metabolism, and the remainder leaves the intra-cellular fluid as protein is utilized (Table I).

Subtracting this water metabolism from the litre of fluid that is lost insensibly we are left with providing an anuric patient with only 400 to 600 ml. of water per day. This quantity, however, is only a guide for it is unwise to stipulate a definite quantity of fluid, because each patient's needs vary according to circumstances. For instance pyrexia alters the amount of water required, and vomiting and diarrhoea may complicate the calculations. The only satisfactory way of assessing the fluid requirements is to weigh the patient daily. In anuria the fluid intake must be adjusted to achieve a daily weight loss of 300–400 g. (10·5–14 ounces).

TABLE I
The Fluid Requirement of an Anuric Patient

	ml.
Insensible loss	1,000
Water of metabolism ($C_6H_{12}O_6 + 6\,O_2 = 6\,CO_2 + 6\,H_2O$) ..	500
Water released from cells	
Fluid required per day	500

The calorie intake of anuric patients is important. It is unnecessary to administer fat as most patients have sufficient reserves in their bodies to satisfy requirements during the anuric phase. This is fortunate because fat is nauseating and unpleasant to take. On the other hand glucose is essential. Some workers suggest that 100 g. of glucose per day will suppress the endogenous metabolism of protein maximally and that larger amounts are unnecessary. It is advisable to give glucose in solution and as the

* Read at the North of England Obstetrical and Gynaecological Society, 17th January, 1958.

fluid requirement is about 500 ml. per day the maximum reasonable quantity of glucose that can be given is limited to 250 g. per day. This quantity often produces nausea and vomiting, and it may have to be reduced, but not below 100 g. per day.

We therefore advocate the adoption of the following dietary regime during the anuric phase:

Glucose ..	..	100–200 g.
Water ..	..	400–600 ml.
Vitamins		

Vitamins are essential and it is advisable to err on the generous side.

Whenever possible this mixture should be taken by mouth. Intragastric drips should be avoided as they are uncomfortable to the patient, making oral hygiene more difficult and, theoretically, may tend to increase the incidence of antibiotic resistant staphylococcal enteritis. The delivery of a 40–50 per cent glucose solution into large veins by means of polythene tubes has a place when fluid and glucose cannot be given into the intestinal tract. Otherwise they should be avoided as the complication rate in this method of the administration of glucose solution is high. This dietary regime, provided it is instituted early, is frequently sufficient to tide a patient over a period of anuria, but once advanced uraemia occurs more energetic treatment is required. It is in these situations that the artificial kidney can play a predominant role.

The Artificial Kidney

The first Artificial Kidney to be used successfully in clinical work was designed by Kolff (1947). At the Peter Brigham Hospital, Boston (Murphy *et al.*, 1952), this machine was modified and improved, and it is this model that we have been using in Leeds since October, 1956. Figure 1 shows the Kolff-Brigham model assembled and filled with its normal working capacity of two pints of blood. This quantity of blood makes sure that no undue circulatory imbalance occurs when the patient's blood enters the machine because a similar volume flows back into the patient. Figure 2 shows the

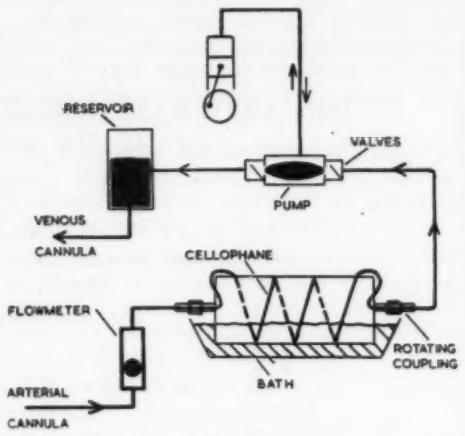

Fig. 2

Diagram of Kolff-Brigham Artificial Kidney (after Merrill, 1955).

machine in diagrammatic form. The radial artery is cannulated, after it has been exposed and dilated with 2·5 per cent papavarine (Parsons and McCracken, 1957), and blood is delivered to the cellophane tube by the arterial pressure of the patient. The rotation of the drum propels the blood along the cellophane tube, which is 160–168 feet long, and it is then pumped from the distal end of the machine into a reservoir, and returned through a cannula inserted into a suitable large vein. The blood in the machine comes into contact with plastic surfaces only, and 14,000 units of heparin, given in divided doses, is used as an anti-coagulant. The original Kolff-Brigham model could only deal with 300 ml. of blood per minute, but the modifications that we have introduced in cannulating the radial artery have given us flow rates of 400–500 ml. per minute, and we have introduced certain modifications to deal with these higher flow rates (Parsons and McCracken, 1958). The functioning unit in the artificial kidney is a semi-permeable membrane consisting of a cellophane tube which separates the patient's blood from a bathing solution. The surface area of the cellophane is approximately 3 square metres, which is slightly greater than the glomerular beds of normal kidneys. The pores of

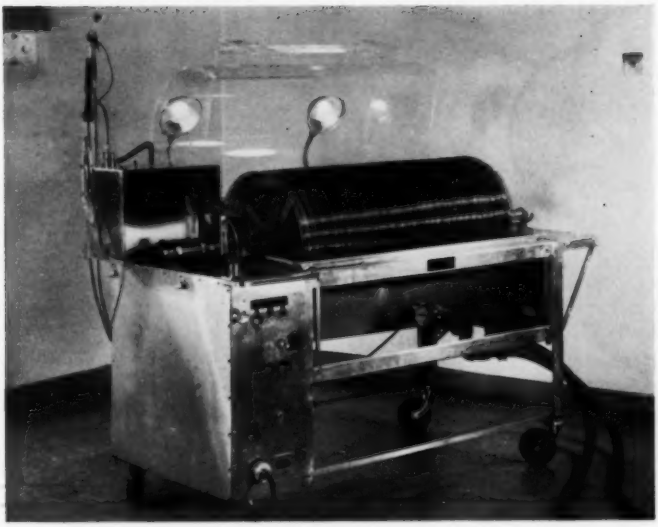

FIG. 1
The Kolff-Brigham Artificial Kidney.

TABLE II

Typical Composition of Bath Fluid

NaCl*	660·0 g.	Ca Acetate	20·0 g.
$NaHCO_3$	225·0 g.	Mg Acetate $4H_2O$	10·4 g.
K Acetate	34·3 g.	Glucose	400·0 g.

Leeds Tap Water 100 Litres

Na*	140·0 mEq/L	Mg	1·7 mg. per cent
K	3·6 mEq/L	Ca	6·0 mg. per cent
HCO_3	27·0 mEq/L	Cl*	113·0 mEq/L

* Adjusted according to plasma level of Na.

the cellophane are too small to allow large molecules such as protein to pass through but smaller molecules pass readily according to the concentration gradient across the membrane. Loss of essential ions from the blood is prevented by adding these to the bath (Table II).

The concentration of potassium in this bath fluid is slightly lower than that used by other workers which usually ensures that the potassium concentration in the patient's plasma at the end of the dialysis is about 4 mEq/L. The volume of fluid in the bath is large and thus the concentration of substances removed from the blood rises slowly. The concentration of these substances in the bath is kept low by changing the fluid every 2 hours. The duration of the dialysis is 6 hours, and a further 2 to 3 hours is required for assembling and dismantling the machine.

During the dialysis both the patient and the machine require constant supervision by a trained staff. It is advisable to have available two doctors, two nurses, and one laboratory technician for the procedure. This allows for certain periods away from the room, and thereby increases efficiency.

Complications

The dangers and complications that can arise from the use of an artificial kidney are few, provided a well-trained team conversant with the procedure is available. Theoretically the most dreaded complication is a mismatch in the blood used to fill the machine. This necessitates a very careful grouping and cross-matching technique. Indeed in 3 of our patients who had had previous transfusions antibodies caused difficulty in the supply of compatible blood. In one obstetrical patient, whom we shall refer to later, the Blood Transfusion Service had to test a total of 150 bottles of Group "B" positive blood before finding four pints that were compatible.

We have had no fatality attributable to the procedure though 3 patients have died during a dialysis. Two of these patients were in uraemic coma, and the third had had a recent operation for an aortic stenosis and he developed an acute cardiac arrest during his second dialysis. The procedure had to be terminated earlier than usual in 5 patients. Two of these developed haemorrhage into a post-operative wound, one developed signs of an internal haemorrhage, another developed an exacerbation of an existing mental disturbance, and the fifth developed a small cerebral vascular accident, which had completely cleared within 48 hours.

Chemical Response

A typical chemical response obtained by dialysis is seen in Figure 3. A high plasma potassium level can be returned to normal values very rapidly by withholding potassium from the bath during the first hour, and in this patient the potassium level was lowered from 7 to 4 mEq/L. The figure shows the gradual fall of the Blood Urea Nitrogen (B.U.N.) and a rise in the CO_2 combining power. Following the dialysis a gradual return to the pre-existing chemical state occurs in anuric patients.

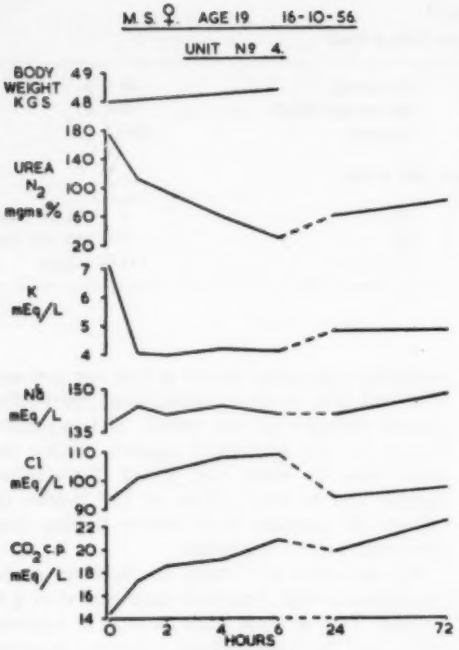

FIG. 3

Chemical response in six-hours dialysis in an anuric patient.

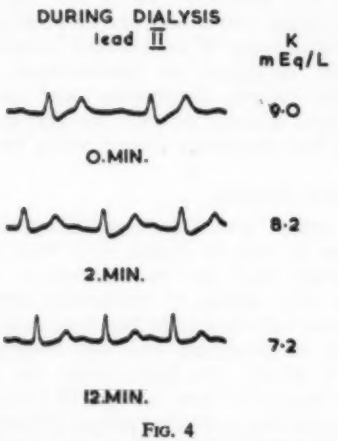

FIG. 4

E.C.G. records during the first 12 minutes of a dialysis in a patient with hyperkalaemia.

Clinical Response

Although chemical improvement occurs during the dialysis the clinical changes are usually delayed from 24–48 hours. Previously present nausea and vomiting cease and the patient becomes hungry. Acidotic respiration disappears. Drowsiness and confusion give place to mental alertness and the patient becomes co-operative. A few improvements, however, do occur during the dialysis. Arrythmias due to potassium intoxication usually disappear within twenty minutes, and E.C.G. changes return to normal very rapidly (Fig. 4).

Indications for Performing a Dialysis

These are varied and no very hard and fast rules can be laid down. Four chief factors are important:

A. *General Clinical Deterioration*

This includes a mental change, persistent vomiting and a falling blood pressure. Deterioration in the clinical condition of patients with anuria frequently occurs rapidly. The patients become unco-operative and difficult to treat. If oral feeding is continued when vomiting becomes pronounced a vicious circle develops, for the uraemia becomes worse and dehydration appears. In the past intragastric or intravenous feeding was instituted but today dialysis is the most effective and surest form of treatment.

It is important to distinguish between vomiting caused by the uraemic state and vomiting caused by a developing intolerance to the dietary regime. Intolerance to the sweet taste of glucose can sometimes be overcome by substituting lactose. Flavouring agents are helpful, and occasionally cooling the glucose in a refrigerator masks the taste.

B. *Potassium*

Elevation of the potassium level of the plasma to toxic levels, which we have arbitrarily chosen as 7 mEq/L. The routine use of cation-exchange resin for hyperkalaemia is not advised.

C. *Alkali Reserve*

Depression of the alkali reserve to levels below 13 mEq/L should be treated by dialysis.

Occasionally, in an emergency, temporary relief can be obtained by giving sodium lactate intravenously.

D. *Urea*

Although urea is to be regarded as a relatively non-toxic substance we have found that levels of the B.U.N. over 200 mg. per cent indicate that the patient is reaching the limit of tolerance.

We have regarded each of these four as an indication in its own right although the first is the most reliable.

Clinical Conditions Suitable for Dialysis

In 6 patients with chronic nephritis we have had no lasting improvement, and at the moment do not consider this disease as a frank indication. Three cases of sub-acute glomerulo-nephritis, presenting with anuria, have been treated. Two diagnosed by a percutaneous renal biopsy have recovered, and a third died.

The remainder of our patients have been grouped under three headings:

A. *Patients Unfit for Diagnostic Procedures*

Seven patients who were later shown to have irreversible renal lesions presented as diagnostic problems. They had such an advanced degree of uraemia that preliminary dialysis was necessary before diagnostic procedures could be completed. One of these patients presented with ureteric obstruction ten years after a Wertheim's hysterectomy. The appearance of a retrograde pyelogram suggested a peri-ureteric fibrosis. Preliminary dialysis prepared the patient for a left nephrostomy. At this operation the ureter was found to be imbedded in fibrous tissue, clinically in keeping with peri-ureteric fibrosis, but a biopsy revealed the recurrence of the malignant disease.

B. *Extra-renal Uraemias*

We have treated 6 patients who developed uraemia as the result of an extra-renal lesion; 5 recovered. In one patient the metabolic response to a major surgical procedure overloaded his diminished renal reserve. Dialysis rapidly improved his condition and he made a satisfactory recovery. The other 5 patients had partial obstructions in the renal tract and dialysis was performed to improve the condition of the patient prior to operation. The one patient that died had a carcinoma of the bladder which was obstructing both ureteric orifices. Preliminary dialysis allowed a left nephrostomy to be carried out but he died following a total cystectomy.

The number of patients in this group is small, but our series so far has been encouraging.

C. *Acute Renal Failure*

The term acute renal failure is chosen in preference to other terms such as tubular necrosis, lower nephron nephrosis, crush syndrome, etc. This is the group in which the artificial kidney is of most benefit. When considering acute renal failure it must be remembered that only the most severe cases have been referred to our unit, the mild ones being successfully managed in their own hospitals by the dietary regime. Of 41 patients with acute renal failure who have been referred to us for treatment on the artificial kidney, 10 were not treated by dialysis. Of these 10, 6 recovered, and 4 died, 3 of them before a dialysis could be attempted. The remaining 31 patients with acute renal failure required one or more dialysis and 18 recovered.

Twenty-one of these 41 patients with acute renal failure were referred by gynaecologists and obstetricians, and the results are summarized in Table III.

Only one of these patients was referred from the Leeds Group of Hospitals, the remainder came from the Midlands, Northern England

Table III

The Results in Acute Renal Failure. Obstetrical and Gynaecological Conditions

	Dialysed		Not Dialysed	
	Total	Re-covered	Total	Re-covered
Abortion	5	5	1	1
Uterine operations	2	1	1	1
Late pregnancy ..	8	8	4	2
Total	15	14	6	4

and Southern Scotland. In the majority of instances the reason for the transfer was a worsening of the clinical condition with advancing uraemia. A few of these patients *might* have survived if the dietary regime had been continued, but this is quite academic for the rapid clinical improvement that occurred after dialysis made subsequent treatment easier and assured final recovery. Of these 19 patients, 3 died. Two of these had complications in the last 3 months of pregnancy. One died half an hour after admission and another will be referred to later. The remaining patient that died required 4 dialyses. She developed an acute renal failure when an intra-abdominal haemorrhage occurred 24 hours after a hysterectomy. She developed an antibiotic-resistant staphylococcal enteritis and septicaemia, but renal function was recovering when she died on the 27th day.

Representative Cases

1. *J.H. Aged 39*

A case illustrating a protracted oliguric phase following a concealed accidental haemorrhage. Recovery.

This patient developed anuria when a concealed accidental haemorrhage terminated her fourth pregnancy at the 32nd week. She was referred to us from Lincoln on her 8th day of illness. She had slow cerebration, had lost interest in herself and in her surroundings, and she was vomiting. The B.U.N. at the time of her admission exceeded 200 mg. per cent, the potassium level in the plasma was nearly 9 mEq/L, and the carbon dioxide combining power was low (Fig. 5). This state developed despite a strict dietary regime having been instituted in Lincoln at the onset of the anuria. The first dialysis improved her condition considerably. She ceased to vomit, she took an interest in her surroundings, and drank the glucose, water and vitamin mixture without any difficulty. Within one week, however, the general clinical condition deteriorated again, and the blood chemistry reverted to almost the same level as at the time of the first dialysis (Fig. 5). The second dialysis was performed. The clinical and chemical response to this second dialysis was again satisfactory, but 9 days later the mental condition started to deteriorate again, the breathing had become acidotic in type and a third dialysis was planned for the following day. Just before connecting her to the artificial kidney a major convulsion occurred. The third dialysis was completed satisfactorily, and she recovered. No excessive diuresis occurred during the recovery phase but replacement therapy with sodium, potassium, and chloride was required because of the urinary loss of these ions. The weight loss during the period of anuria averaged 380 g. per day, whilst the fluid intake was 400 ml. per day. During the recovery phase on an unrestricted diet the patient gained weight at a

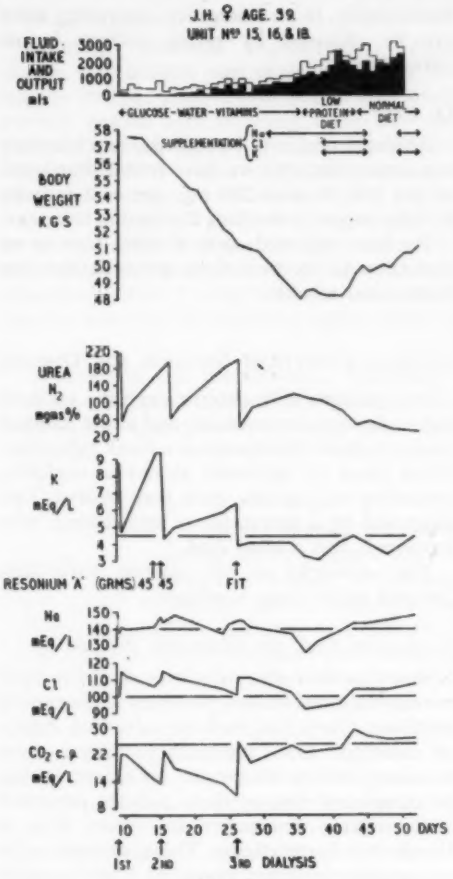

FIG. 5

Case 1. The responses in an anuric patient who had a concealed accidental haemorrhage.

constant rate and this suggested that no undue overhydration or dehydration had occurred over the period of anuria.

She was reviewed three months later. Her blood chemistry was normal and the urea clearance was 50 per cent of normal. Clinically she was well but it had taken nearly three months for her normal health and strength to be restored.

2. *K.B. Aged 29*

An anuric patient illustrating the treatment for acquired haemolytic anaemia occurring after a massive transfusion of blood. Recovery.

This patient was a para-4 who started to bleed profusely at the 39th week of pregnancy. Three pints of blood were transfused in her own home and a total of 12 to 15 pints were given before a lower segment Caesarean section had been performed for placenta praevia, type 4. A prolonged period of hypotension accompanied this episode. The child survived. She became anuric and was transferred to Leeds from Hull 3 days after the Caesarean section had been performed. On this day her haemoglobin was 53 per cent and she was jaundiced. Within 48 hours, despite a further transfusion of blood, her haemoglobin had fallen to 25 per cent. Methaemalbumin was detected in her plasma. We made a diagnosis of acquired haemolytic anaemia and gave 100 mg. of hydrocortisone intravenously and then a daily maintenance dose of Cortisone (Fig. 6). Although this stopped the haemolysis she was in urgent need of a further blood transfusion. The Blood Transfusion Service reported three abnormal antibodies (later a total of five were identified), and after they had checked 150 bottles of Group "B" Positive Blood they found only 4 that were compatible. At this time the blood B.U.N. was high (216 mg. per cent, Fig. 6) and in view of the difficulty of obtaining further supplies of compatible blood we decided to use the artificial kidney using two of the available four pints of blood to fill the machine. The red cells of the remaining 2 pints of blood were given at the conclusion of the dialysis. After 3 hours dialysis she developed a small cerebral vascular accident, and the dialysis was terminated as a safety precaution. Forty-eight hours later the cerebral condition had returned to normal. Four days after the dialysis renal function started to return (Fig. 6) and shortly afterwards the uraemic manifestations had subsided. The jaundice and methaemalbumin disappeared shortly after the administration of cortisone. Although the haemoglobin level continued to fall after the dialysis, further transfusions of blood seemed unwise. As the uraemia decreased the reticulocyte count increased and the haemoglobin started to rise as the result of her own haemopoietic activity. The dose of cortisone was then reduced slowly and finally 40 units of A.C.T.H. were given on successive days. She made a satisfactory recovery. Nine months later she wrote to us from Plymouth saying that she was very well.

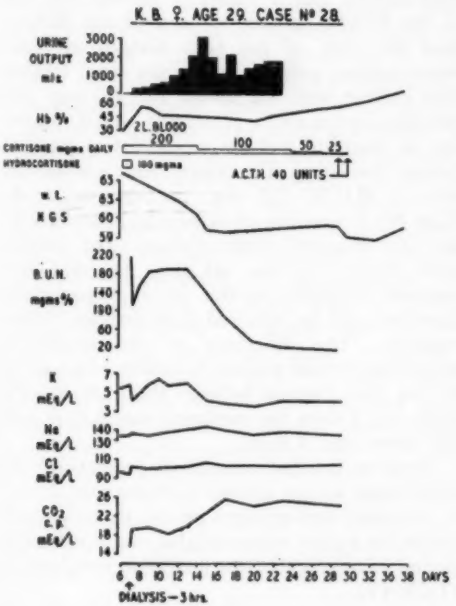

FIG. 6

Case 2. The responses in an anuric patient who developed an acquired haemolytic anaemia following haemorrhage from a placenta praevia.

3. *E.M.T. Aged 39*

A case illustrating the use of the artificial kidney in a patient who had an abortion. Recovery.

Anuria occurred when this 4th para injected soap and water *per vaginam* at the 17th week of pregnancy. About 10 hours later a 9-inch foetus and placenta were expelled. No hypotension was recorded during this episode. Initially she had 300 g. of glucose and 700 ml. water daily, and was transferred to the Artificial Kidney Unit from another hospital in Leeds on the 5th day of anuria (Fig. 7). On admission she was vomiting, and had become mentally depressed. A dialysis lasting 6 hours was carried out on the 6th day of anuria, when the blood chemistry findings were: B.U.N. 120 mg. per cent; K 5·1 mEq/L and CO_2 combining power 15·2 mEq/L. Vomiting continued for 36 hours after the dialysis, but she then took the glucose, water and vitamins orally. From the 7th to the 9th day 600 to 700 ml. of water were given but little loss of weight was recorded (Fig. 7). The fluid intake was then reduced to 400 ml./day plus the volume of urine passed. The weight loss then averaged 500 g./day even though an unrestricted low protein diet with ionic supplementation was given (Fig. 7). The patient started to gain weight at a constant rate from the 28th day.

The urine output increased rapidly after the 12th day, but the B.U.N. did not start to fall until the 19th day. The maximum urine output during the recovery phase was 2,800 ml. per 24 hours.

One year later this patient was alive and well.

Assessment of Severity of Acute Renal Failure

Many patients with acute renal failure survive without haemodialysis, and it is of interest to try and analyze why some patients require dialysis and others do not.

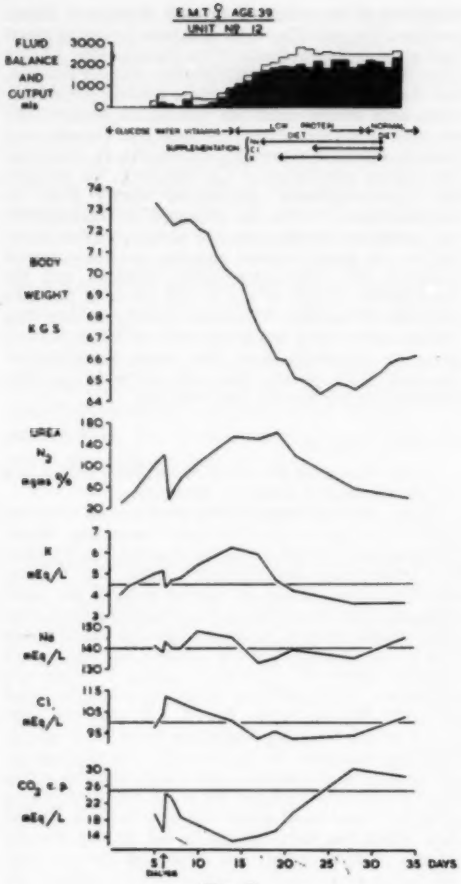

FIG. 7

Case 3. The responses of an anuric patient who had an abortion.

Firstly those that require dialysis may have had inadequate treatment at the onset of the anuria or they may have an unduly protracted period of anuria lasting longer than say 2 to 3 weeks.

Secondly we have been impressed by the different rates by which protein is broken down during the anuric phase. We have estimated this by following the daily rise in the blood urea nitrogen. Our observations suggest that in subjects given an anuric regime the minimum

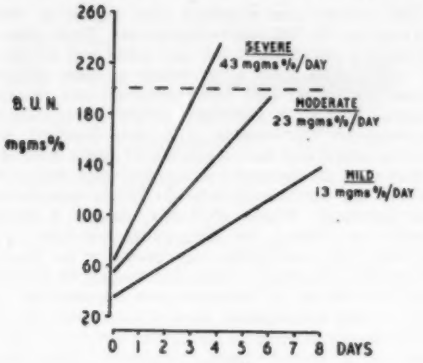

FIG. 8

The rise in the B.U.N. in three representative patients with acute renal failure.

rise in the blood urea nitrogen is in the order of 5 to 9 mg. per cent per day (Parsons and McCracken, 1957). Figure 8 records the rise in the B.U.N. between the end of one dialysis and the start of the next dialysis in three representative patients with acute renal failure. The patient with the lowest rise (13 mg. per cent/day) developed a protracted anuria following an abortion and she required two dialyses before recovering. The patient with a moderate rise of B.U.N. (23 mg. per cent/day) was Case No. 1 who had an accidental haemorrhage and she required three dialyses. The patient with the severe rise (43 mg. per cent/day) received multiple injuries in a motor cycle accident, and he required four dialyses before recovery. The difference in the metabolic responses of these patients is further emphasized by the time interval between the dialyses—the mild case 8 days, the moderate case 6 days and the severe case 4 days.

We have classified our patients presenting with acute renal failure according to the rate of rise in the blood urea nitrogen per day in those cases where the figures were available over a sufficient period of anuria to draw justifiable conclusions (Table IV).

In the *mild* group where the rise in B.U.N. was less than 15 mg. per cent per day 2 of the patients required dialysis out of the 7 referred to us. We believe that in this mild group the dietary

TABLE IV

Daily Rise of B.U.N. in Acute Renal Failure

Degree	Daily Rise in B.U.N. (mg. per cent)	No. of Patients	No. Dialyzed	Recovered
Mild ..	15	7	2	7
Moderate	15–30	13	12	9
Severe ..	30	10	10	3

regime seems to be adequate, the artificial kidney being reserved for those patients whose anuric phase exceeds 2 to 3 weeks or where the dietary treatment has not been correctly instituted.

In the *moderate* group (where the B.U.N. is rising between 15 and 30 mg. per cent per day), we have observed 13 patients, 12 were dialyzed and 9 recovered. The one that died without a dialysis having been performed had had an accidental haemorrhage at the 32nd week of pregnancy, and was the second patient with acute renal failure that we treated after receiving our artificial kidney. She developed a high serum potassium level which was lowered by ion exchange resins. Later a very severe pulmonary oedema occurred and a convulsion. In other words we had allowed her to progress too far without performing a dialysis, the B.U.N. had reached 180 mg. per cent just before death on the 11th day of her anuria. The other patient who died in this group was dialyzed and the uraemia was corrected. On admission he was overhydrated and he died from a severe pulmonary oedema. It seems that in this moderate group the artificial kidney is probably necessary for survival. With one exception all of those patients who had been referred to us following a concealed accidental haemorrhage have fallen into this moderate group.

The *severe* group (where the B.U.N. is rising in excess of 30 mg. per cent/day) offers a far greater challenge to clinical and biochemical control. Ten patients were treated, all were dialyzed but only 3 recovered. Most of this group had received extensive trauma, either accidentally or from a major surgical procedure. The resulting renal lesion was therefore only one aspect of the clinical problem. Complications of the primary lesion were frequent and these were undoubtedly made worse by the uraemic state.

Infection, which increases the metabolic response, plays an important role. In acute renal failure the resistance to infection seems to be reduced and in many instances, despite the recovery of renal function, the patient has died from overwhelming infection. The healing of wounds is retarded and in two patients disruption of an abdominal wound has occurred. Infections caused by antibiotic-resistant strains of staphylococci have played a predominant role in the management of this severe group of patients. Indeed 3 of those who died developed overwhelming infections from these organisms. The infection seems to attack in particular the alimentary tract and staphylococcal enteritis is one of the most dreaded complications in the management of patients with renal failure. It is not confined to those patients treated on the artificial kidney. The majority of cases that have developed staphylococcal enteritis have received broad spectrum antibiotics. The prophylactic use of antibiotics in anuric patients must be condemned and they should only be used to combat established known infections. When antibiotics are given to patients with mixed bacterial infections repeated investigations are required lest the growth of only one organism is controlled. The other organism may then grow more rapidly. This seems to be particularly important in pulmonary infections. We now have sufficient evidence to show that many patients have these antibiotic resistant strains of staphylococci already resident in their noses and faeces on arrival from other hospitals.

In the severe group of patients with acute renal failure we suspect that factors other than infection tend to reduce the chances of survival. Calculation reveals that these patients break down their own proteins 4 to 10 times faster than would a normal individual receiving an anuric diet. The break-down of fat is probably excessive too, and this rapid catabolism may well lead to a severe nutritional depletion. Further, repeated dialysis which is often required in this group may aggravate the nutritional depletion by removing essential substances from the body. This aspect in the nutritional state has certain practical

applications. For instance several patients have developed persistent vomiting after renal function had recovered. Five hundred to 1,000 ml. of milk per day has frequently stopped the vomiting in these patients though it may have to be given by intragastric drip and chlorpromazine used to suppress the vomiting. This suggests that a nutritional depletion can occur during the anuric phase though the specific deficiency has not been ascertained.

In retrospect many of these severe cases have probably been referred to us too late and earlier transfer may improve the prognosis. It is essential to recognize these patients early. The majority have received major trauma and an initial rapid rise in the blood urea and serum potassium levels should give ample warning of the severe metabolic response. These patients should be moved to an Artificial Kidney Unit as soon as the severity is recognized. As the B.U.N. may be rising in this severe group at 50 mg. per cent per day this transfer may be necessary as early as the second or the third day of the illness. Incidentally a similar situation confronts us after the first dialysis and the second may be necessary within three or four days. In our severest case, who had had a hysterectomy, the B.U.N. was rising at 80 mg. per cent per day, and the second dialysis had to be performed within 48 hours of completing the first.

Conclusion

We believe that the artificial kidney is a safe and reliable method for the treatment of selected cases of acute renal failure. The procedure is time consuming. Developing an Artificial Kidney Unit is expensive and complicated and a highly trained team is required that can be spared from normal hospital routine. Furthermore, to maintain optimum efficiency, the artificial kidney should be used at fairly frequent intervals and as suitable cases are not common it would seem undesirable to have too many machines in this country. In support of this we have found that transportation of these patients is quite feasible, provided it is done early. Early transfer also allows detailed assessment to be made as to the most opportune time to perform a dialysis.

Summary

(1) The dietary treatment of acute renal failure is outlined.

(2) The Kolff-Brigham Artificial Kidney is described.

(3) The chemical and clinical response to dialysis is given.

(4) The results obtained in 63 patients (21 referred from obstetricians and gynaecologists) are presented.

(5) The indications for performing a dialysis are outlined.

(6) It is suggested that patients with acute renal failure should be classified as mild, moderate or severe according to the metabolic response.

The artificial kidney was bought and is being maintained by the Board of Governors of the United Leeds Hospitals.

We wish to thank all the consultants who have referred cases to our unit. We are grateful to Mr. J. B. Farquhar for help and advice in the treatment of some of the obstetrical and gynaecological cases.

Figures 2, 3, and 5 are published with the kind permission of the Editor of the *British Journal of Urology*.

We thank Mr. J. Hainsworth, Department of Medical Photography, St. James's Hospital, Leeds, for Figures 1, 4, 6, 7, and 8.

We wish to record that Mrs. S. M. Hobson, A.I.M.L.T., and Sister M. Thwaites have been, from the beginning, members of the team operating the artificial kidney, and the successful operation of the machine has depended considerably on their efforts.

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RETICULUM CELL SARCOMA IN PREGNANCY

BY

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THIS case is considered to be of interest because of the comparative rarity of the reticulum cell sarcoma, particularly in association with pregnancy.

The sarcoma, which was first described by Roulet in 1930, is one of the three main groups which constitute the tumours of lymphoid tissue, the other two being lymphosarcoma and Hodgkin's disease. All three groups of tumours arise from primitive mesenchyme and many present a mixed cytological picture which often makes it difficult to put them into any one category. This partly explains why there are so few references in the literature to reticulum cell sarcoma in pregnancy. The histological diagnosis is further complicated by marked variation in the degree of differentiation of reticulum cell sarcoma.

Lumb (1952) reported six cases of reticulum cell sarcoma in a series of 176 tumours of lymphoid tissue, an incidence of 3·4 per cent. More recently, with Newton (1957) he reported 29 cases in a series of 376, an incidence of 7·7 per cent. There is a higher incidence of the tumour in males and it tends to occur more commonly in the older age groups. In the latter series the average survival period was less than 2 years but 4 cases, 13·8 per cent, survived more than five years.

The only other case of reticulum cell sarcoma in pregnancy which it was possible to find in the literature was reported by Heseltine and Loth in 1956. In this case the primary site was in the thymus gland.

CASE HISTORY

Mrs. E.C., aged 27, attended the surgery in January, 1956, giving a history of 6-weeks amenorrhoea. The expected date of delivery was calculated as 29th August, 1956.

This was her third pregnancy. Her first pregnancy ended in a normal delivery, at about 35-weeks' gestation, of a living male child weighing 3 pounds 4 ounces. This child is now alive and well. Her second confinement took place at home, in 1954, when she was delivered—again at about the 35th week of pregnancy—of a living male child weighing 3 pounds 8 ounces. The total duration of this labour was approximately 2 hours. The baby was transferred to hospital 25 minutes after birth but survived only 21 hours. The cause of death was atelectasis associated with prematurity.

Shortly before her second pregnancy, in 1954, the patient complained of a pain in her left thigh, she had a troublesome cough and she had been losing weight. A full clinical examination revealed no abnormal physical signs apart from a total shift of her lumbar spine to the left. X-ray examination of her chest, lumbo-sacral spine and pelvis revealed no abnormality except a small enchondroma in the body of the second lumbar vertebra. This enchondroma did not alter in shape or appearance in any subsequent examination and was thought to be benign. She was sent for a period of convalescence after which her general condition improved. She remained, however, subject to intermittent episodes of pain in her left thigh and left sacro-iliac region.

Twelve months after her second confinement, that is, in July, 1955, she complained of lassitude and she had lost one stone in weight during the preceding 12 months despite a good appetite. She was admitted to hospital for investigation and was found to have a macrocytic anaemia (haemoglobin 77 per cent, red blood corpuscles 3·6 million per ml., white blood corpuscles 7,800 per c.ml.) but apart from this no other cause could be found for her symptoms.

In her third, and last, pregnancy her last menstrual period commenced on the 22nd November, 1955. Because of her two previous premature deliveries she was referred to hospital to be booked there for confinement. In the absence of any definite clinical picture her anaemia and loss of weight, as well as the two premature confinements, were ascribed to malnutrition. She was given oral iron and folic acid and asked to attend the hospital antenatal clinic regularly throughout pregnancy.

In March, 1956, she presented herself at the practice antenatal clinic complaining of a severe low backache. The pain was so intense that she could not endure sitting at the hospital antenatal clinic for any length of time. On examination she exhibited definite signs of left sciatic nerve irritation with half an inch of wasting of the left thigh (as compared with the right). An orthopaedic

opinion was sought but no cause for these signs and symptoms could be found. X-ray examination of the sacro-iliac joints and left hip joint showed osteitis condensans ilii of the left sacro-iliac joint but no other bone abnormality (Fig. 1).

There was no improvement during the next four weeks and she was admitted to hospital for double leg traction. She improved rapidly while in hospital and was discharged after 3 weeks and supplied with a maternity corset. This corset together with mild analgesics maintained her in a comfortable condition throughout the remainder of the pregnancy. By May, the sixth month of her pregnancy, her haemoglobin had risen to 80 per cent.

On 4th July she was admitted to hospital, in labour. She was then in the 32nd week of pregnancy. After a labour lasting 4 hours and 25 minutes she was delivered of a male child weighing 3 pounds 12 ounces who is now alive and well. The patient was discharged from hospital on the 10th day of the puerperium but the baby remained in hospital a further 4 weeks until his weight was 5 pounds 8 ounces.

Nine weeks after delivery the patient attended for her postnatal examination; the main reason for her coming was a recurrence of her backache. Vaginal examination revealed an involuted and retroverted uterus and some tenderness in both vaginal fornices. No mass was palpable in either fornix but the patient did not relax throughout the examination. Examination of her left hip joint showed some spasm of the surrounding muscles; she was also unable to bear weight on her left leg. She was readmitted to hospital for investigation of her neuropathy but shortly after admission a palpable lymph gland was detected in the left inguinal region. Within 2 weeks a mass was palpable above the left inguinal ligament. Neither the liver, the spleen nor any other lymph gland was palpable, rectal and vaginal examination were negative and a differential blood count gave no useful information. A differential diagnosis of a tuberculous lesion or Hodgkin's disease was made, and an exploratory operation was performed. Through an incision parallel to the left inguinal ligament a mass of enlarged lymph glands was seen to be lying along the external iliac vessels. These glands had the macroscopic appearance of Hodgkin's disease and a group of them was excised leaving the main mass *in situ*. Histological examination revealed a reticulum cell sarcoma (Fig. 2).

The patient developed a post-operative bronchopneumonia from which she recovered. She was then given a course of high voltage X-ray therapy but during treatment a nodule appeared in the skin within the area of treatment and continued to grow despite the irradiation. The tumour, therefore, was considered to be insensitive to X-rays and the patient was discharged home.

The remaining 2 months of her life saw a rapid deterioration in her condition. She was subject to hot flushes, presumably due to the irradiation of her ovaries, and palpable lymph glands appeared in the right inguinal region, the axillae and the neck. The terminal stages were complicated by pressure on the trachea by enlarged mediastinal glands. She died on the 7th February, 1957, 7 months after her third confinement.

Permission for a post-mortem examination was refused but, from the operation findings and from the clinical picture, it can reasonably be assumed that the primary site lay in the retro-peritoneal space. Tumours in this area generally give rise to few symptoms until they have reached a large size.

Comments

The predominant symptom in this case was severe left-sided sciatic pain for which no cause could, at first, be found. Donnelly (1946) analysing 95 cases of primary retroperitoneal tumours does not include sciatic pain amongst the symptoms but Way (1951) points out that sciatic pain, which is the commonest type of pain in carcinoma of the cervix, is always associated with involvement of the pelvic lymph glands on the side on which the pain is experienced.

Young (1940), discussing pelvic arthropathy in pregnancy, emphasizes that sacro-iliac disease may produce a marked degree of incapacity. Osteitis condensans ilii must be included in pelvic arthropathy and Thompson (1957), reviewing this condition, states that it commonly occurs in parturient women often affecting only one side. The chief symptom of osteitis condensans ilii is pain in the distribution of the first and second sacral nerves.

The sciatic pain, therefore, may have been due to direct involvement of the nerve trunks by the malignant cells, which accounts for the marked wasting of the left thigh, or it may have been due to sacro-iliac disease which would explain the alleviation of the pain following double leg traction and while she was wearing a maternity corset. It is probable that both were factors in the causation of the sciatic pain.

Three years elapsed between the onset of the sciatic pain and the death of the patient, and shortly after the onset of the pain the patient began to lose weight. It would appear, therefore, that the tumour was present not only during the last pregnancy but also during the second one. Although the reticulum cell sarcoma, generally, has a poor prognosis, 13·8 per cent of the second series quoted above survived more than 5 years. The salient features of these cases, and which were present in this case, were the localization of the tumour mass and the absence of deterioration of general health.

FIG. 1

Left sacro-iliac joint showing osteitis condensans ilii.

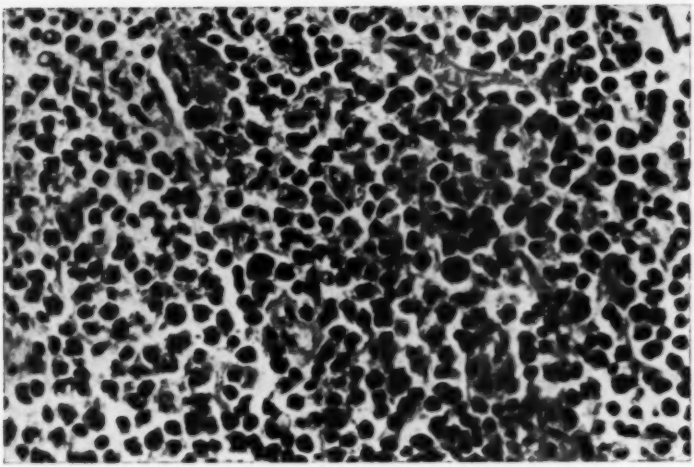

FIG. 2

Reticulum cell sarcoma. ×500.

SUMMARY

A case of reticulum cell sarcoma occurring in association with pregnancy is described. The absence of localizing signs and symptoms is mentioned and the causation of the sciatic pain is discussed.

I wish to thank Professor T. N. A. Jeffcoate and the consultant staff of Newsham General Hospital and the Liverpool Radium Institute, under whose care this patient was, for access to the case records and permission to publish, and to Mr. H. H. Francis for his helpful advice.

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DELIVERY BEFORE FULL DILATATION WITH SPECIAL REFERENCE TO INCISION OF THE CERVIX

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WHEN delivery of the child becomes necessary or desirable before full dilatation of the cervix the choice can only be Caesarean section or incision of the cervix and forceps delivery. Caesarean section is a popular, straightforward method with much to commend it, but it is not without risk to life and health, and it can be difficult. If less damaging methods are available they should be used. There are a number of occasions when incision of the cervix and forceps delivery is simpler and safer than Caesarean section, and is not the mutilating, traumatic, and dangerous procedure that some would have us believe (Stansfield and Drabble, 1951).

A number of papers have been written in recent years describing its use in this country (O'Sullivan, 1939; Fitzgerald, 1949; Corbett, 1952; Cope, 1955) and in the U.S.A. (Douglas and Graves, 1948; Evans and Stander, 1954; Rubovits and Cooperman, 1955) but it is evident that opinions differ as to when it should be employed. Jeffcoate (1955) considers that it should probably be restricted to cases of cervical dystocia, and Cosgrove (1948) has condemned it except on the very rarest occasions. Moir (1956) contrasts those who "strain at a gnat" and recoil from cutting the thinned out cervix with those who "swallow a camel" and do not hesitate to make deep perineal incisions. Theobald, Kelsey and Muirhead (1956) commend the operation in the management of certain cases of prolonged labour.

It is clearly necessary that the indications, difficulties, and dangers of this mode of delivery should be understood before embarking on it, and to this end we have reviewed our experience of it during the last few years. We now present our results, describing in some detail the different circumstances leading to its use, and we do this because we are convinced that in favourable conditions cervical incision and forceps delivery is easier for the obstetrician, at least as safe for the child, and causes less damage to the mother, both immediate and late, than Caesarean section.

RESULTS

We have studied the records of 44 cases conducted by us or under our supervision in the Jessop Hospital and in the University Unit at the City General Hospital, Sheffield, since 1951. It is estimated that some 12,000 deliveries occurred during the same period; i.e. an incidence of 0·37 per cent. Except for 2 cases in which the foetus died early in labour, all the babies were born alive (including 2 sets of twins), and made normal progress (Table I). Many were above average weight, 22 being over 8 pounds and

TABLE I

Results of Delivery before Full Dilatation

Total cases	44
(Total Deliveries (approximately) ..	12,000)
(Incidence	0·37 per cent)
Live births (2 sets of twins)	44
Died early in labour	2
Foetal loss due to delivery	0

TABLE II

Birthweight after Delivery Before Full Dilatation

No. of cases	Weight in pounds			
	up to 7	7 to 8	8 to 9	9 to 10
Foetal distress ..	2	2	4	–
Cervical dystocia ..	1	2	–	–
Prolonged labour ..	8*	11	10	6
Total	11	15	14	6

* Includes 2 sets of twins.

7 over 9 pounds at birth (Table II). There were no serious maternal complications. The operation has usually been easy and has not been followed by shock. None of our patients has been more upset than by an ordinary forceps delivery. Bleeding from the cut edges of the cervix has always been slight. We have never seen dangerous extension of the incision into the vaginal vault, nor into the lower uterine segment.

Post-operative infection has not been a significant problem. Ten of the 44 mothers were given chemotherapy in the puerperium, or had a notifiable pyrexia, but 6 of these were very mild infections and 4 of them proved to be extragenital in origin. Only 4 of the 44 patients had a material genital tract infection, and all but one of these had been admitted as emergencies after many hours of delayed labour. All recovered completely within a few days. The most severe, delivered after 102 hours hypotonic inertia, the first 3 days of which were at home, developed a *Escherichia coli* septicaemia after delivery. She made a good recovery, and 3½ years after the labour referred to, in January, 1958, she had an easy normal labour lasting 12 hours.

CONDITIONS TO BE SATISFIED

The conditions considered necessary before we contemplate this operation are largely those occurring late in labour, when the head has reached the pelvic floor, and were it not for the thinned portion of cervix remaining, none would hesitate to deliver with forceps. These conditions may be summarized as follows:

(1) The head is deeply engaged.

(2) The vaginal vault is fully dilated.

(3) The cervix is thin, and the vagina below the presenting part is distensible.

(4) The bony outlet is adequate, and no other obstruction exists.

Dilatation of the vaginal vault can be recognized by passing the fingers outside the undilated portion of cervix into the lateral vaginal fornices and appreciating that they are situated above the greatest convexity of the head (Fig. 1). The importance of this has also been emphasized by Fitzgerald (1949) and Cope (1955). Unless moulding is extreme, the vaginal vault will usually be fully dilated when the leading point on the head has descended a little below the level of the ischial spines. It is also desirable that the vagina below the presenting part should be elastic or capable of being enlarged by episiotomy.

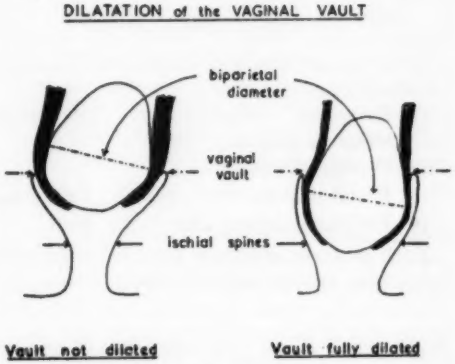

FIG. 1

Diagram showing the relationship of the widest diameter of the foetal head to the fascial tissues of the vaginal vault. Note that the vaginal fornices reach well beyond the greatest diameter of the head when the vault is fully dilated.

Technique

We usually cut the cervix with scissors at 3 o'clock and 9'clock for about ½–1 inch, either under direct vision or directing the blades by touch. This site for division has been selected, as it is here that spontaneous tearing usually occurs (Cope, 1955) and as it is well clear of bladder and rectum. We sometimes incise the cervix before, and at other times after whatever other manipulation is required; in a few instances when the tissues are particularly elastic it is possible to push up the cervix over the head without cutting it at all. After completing the delivery the fornices and lower uterine segment are explored to exclude any other damage; the incisions are then repaired with interrupted catgut sutures.

Table III

Clinical Groups Delivered Before Full Dilatation

	No. of cases
Prolonged labour with impending maternal distress	31
Cervical dystocia	3
Foetal distress (including prolapse of the cord)	8
Prolonged labour after foetal death	2
Total cases	44

Type of Case

Four varieties have been dealt with in this way (Table III):

(1) Prolonged labour with impending maternal distress.
(2) Cervical dystocia.
(3) Foetal distress with prolapse of the cord
(4) Prolonged labour after foetal death.

Each of these groups is now described with summaries of representative case histories.

Prolonged Labour with Impending Maternal Distress

This group is the largest, consisting of 31 cases in which delay was due to weak or inco-ordinate uterine action. Labour lasted for more than 48 hours in 20 of them (average duration of these, 82 hours, Table IV). Progress was often extremely slow, especially during the later hours of observation. In many, the foetal head had reached the level of the ischial spines, and the cervix half dilatation or more within the first 24–36 hours, but little or no advance was recorded during the next day or two, until deterioration in the mother's condition made action necessary. Two typical case records follow:

Table IV

Duration of Labour

Number of cases	Time in hours			
	0–24	25–48	49–72	73–132
Foetal distress ..	6	2	–	—
Cervical dystocia ..	2	1	–	—
Prolonged labour ..	–	11	8	14
Total ..	8	14	8	14

Average duration: 69 hours

Case 1

Mrs. D.W., aged 30, primigravida, was admitted as an emergency after 5 days in labour at home. The foetal head was on the pelvic floor with its widest diameter below the level of the vaginal fornices and the cervix was three-quarters dilated with a thick anterior lip. The mother was tired and acetone was present in the urine so a sedative was given and a litre of 10 per cent dextrose intravenously. Twelve hours later, no change having occurred in the state of the cervix or position of the head, manual rotation from a lateral position and application of forceps was followed by incision of the cervix and delivery. The child weighed 8 pounds 5 ounces and was in good condition. The original ½-inch incision in the cervix, though it had extended to 2-inches long, ended some way from the fornix and was repaired. Recovery was uneventful.

This mode of delivery was particularly helpful when the need arose during long labour in 2 cases of twin pregnancy, as the smaller babes required less dilatation of cervix and vagina.

Case 2

Mrs. M.J., aged 36, primigravida, had a twin pregnancy complicated by toxaemia for which surgical induction was performed at the 38th week. Labour began but the contractions were weak, and after two days and nights, though the leading head was low, the last inch of cervix remained undilated. As there had been no apparent

progress for the last 18 hours, the cervix was incised and the first twin delivered with forceps. The second twin was extracted by the breech, the placenta manually removed, and the cervix repaired. Both babies were healthy and weighed 3 pounds 13 ounces and 4 pounds 8 ounces respectively.

Cervical Dystocia

Occasionally the undilated cervix may be the only barrier to delivery, the uterus in other respects functioning normally. We have chosen to restrict our use of the term to this type of case though it is probable that cervical faults contribute to other forms of disorderly uterine activity. With this restriction in mind it is to be expected that simple cervical incision should lead to spontaneous delivery within a short time. Two cases in this series behaved in this way; both were women in whom cervical erosions had been previously treated by cautery. Incision was followed by delivery in 25 minutes in one, and 3½ hours in the other. The following is a summary of the first of these.

Case 3

Mrs. A.M., aged 30, para-1—previous forceps delivery—had a deep cervical cautery in 1955. She later attended the gynaecological clinic complaining of infertility, and investigation showed an extreme degree of cervical stenosis preventing the passage of a fine probe. She was admitted to hospital and the cervix was dilated, in March, 1956. She conceived shortly afterwards and in due course began in labour at the 41st week. When the head was low in the pelvis further advance was prevented by a hard, stenosed cervix barely half dilated. The stenosed area was cut with scissors, and normal delivery of a healthy child weighing 7 pounds took place 25 minutes later.

Another patient who might be included in this group had a rigid incompletely dilated cervix after nearly two days in labour. Incision was decided upon, but spontaneous laceration occurred during the 30 minutes preparation for operation. She had an easy low forceps delivery and the torn cervix was repaired.

Foetal Distress and Prolapse of the Cord

In this group it is especially important to insist upon the conditions for safe delivery already described as there is a risk that an incautious decision may be made in the heat of the moment.

It has been alleged that incision of the cervix is "very seldom justified in the interests of the foetus. If the foetus is already so distressed as to make its delivery urgent it is ill-equipped to stand the shock of a vaginal delivery of this type" (Morris, 1957).

That good results are possible is shown by our experience of eight cases, 2 with prolapse of the cord, treated by immediate forceps delivery before the end of the first stage without loss of a child or damage to a mother except for an incised cervix promptly repaired.

Case 4

Mrs. J.J., aged 23, primigravida, developed toxaemia at the 37th week for which labour was induced by rupture of the membranes. About 4½ hours after the onset of contractions the foetal heart rate suddenly plunged to 80 beats a minute. The head was very low and the cervix three-quarters dilated, and some bleeding following examination suggested an accidental haemorrhage. Vaginal delivery was judged possible because the vault was supple and fully dilated, so a pudendal block with ½ per cent lignocaine was performed immediately. By the time this was completed the foetal heart rate had fallen to 40 beats a minute and was almost inaudible. The cervix was elastic and, after application of forceps, it could be pushed up over the head so that incision was unnecessary. A cyanosed baby weighing 5 pounds 5 ounces with a slowly beating heart was delivered easily, and quickly recovered. The placenta showed evidence of a recent substantial haemorrhage.

This case was a particularly good example of the occasional overwhelming advantage of delivery before full dilatation over Caesarean section; it is most unlikely that the latter operation could have been arranged and completed quickly enough to save the baby. The risks of Caesarean section, already greater than those of vaginal delivery, are considerably increased when a rushed operation is performed on an ill-prepared patient.

Very occasionally, even if the foetal head is high and the vault not yet completely dilated, immediate delivery can be achieved with safety. It is essential if this is to be done that both cervix, vault, and vagina should be exceptionally elastic and distensible—as for example after the birth of the first twin, or in a woman who has previously borne many children. The only two occasions on which we have departed from the conditions laid down earlier were cases of prolapsed cord in multiparous women.

Case 5

A para-7, with a history of normal births, went into labour at term with the foetus lying obliquely. The head was easily brought over the pelvic brim but remained mobile and tended to float away towards the left iliac fossa. After a short period of labour the membranes ruptured spontaneously and on vaginal examination a loop of cord was discovered prolapsed into the vagina with the head just entering the brim in the left occipito-anterior position. The cervix was three-quarters dilated and very soft and elastic, the vagina also being slack and distensible. Under general anaesthesia forceps were applied within the cervix and, as the head was brought down, the cervix was pushed up above it, and delivery was completed without difficulty and without damage to mother or child (which weighed 9 pounds).

Prolonged Labour after Foetal Death

Two cases occur in this series in which the foetus died early in labour. A special hazard may be involved if this event is followed by over-long delay in the first stage, because the obstetrician is reluctant to use Caesarean section when the baby is already dead and the mother is not in immediate danger; but escape of the liquor and moulding of the uterus round the foetus may lead to a situation in which the mother's life is threatened. To wait for full dilatation may be a hopeless proposition. If excessive retraction of the uterus begins and "active retention" of the foetus is imminent, procrastination and probable operation later on a mother, whose condition has deteriorated, is in no way to be compared with earlier incision of the cervix and delivery. Like Rudolph and Fields (1947) we do not consider this operation suitable for cases of constriction ring dystocia.

Case 6

Mrs. M.K.P., aged 24, a primigravida, was admitted in labour at term with moderately severe toxaemia. The head was engaged and the cervix effaced but not dilated. During the night the foetal heart sounds disappeared. Progress was slow, the patient suffering much backache, until 82 hours after labour began she wanted to bear down. On examination, though the head was very low, occiput posterior, the cervix was irregularly thickened with a very hard rim and was only half dilated. Relaxation between contractions was poor and a palpable retraction ring was forming half-way to the umbilicus. As progress had virtually ceased and tonic contraction threatened, further delay was judged dangerous. Rotation was avoided in view of the irritable behaviour of the uterus. The head was perforated and a child weighing 7 pounds 7 ounces extracted with forceps without difficulty. Blood loss was scanty and 2-inch cervical tears at 3 and 9 o'clock were repaired. The mother made an excellent, apyrexial recovery, and three years later had a normal delivery of a healthy child weighing 8½ pounds after only 8 hours in labour.

Follow-Up

The appearances of the cervix, as judged by inspection 10 days and 6 weeks post-partum have been most satisfactory, but in order to find out what remote ill-effects have occurred, we recently interviewed and examined as many of these patients as we could.

7 had been delivered too recently for examination to be of much value.

19 failed to reply to our enquiry.

2 wrote to say they were well and had no symptoms.

16 were seen and examined.

Of the 12 patients attending for interview who had been operated upon three or more years ago (and had therefore had reasonable time for another pregnancy), 4 have had easy normal labours since lasting 12, 12, 8 and 19 hours respectively. Another who had her cervix incised more recently had again become pregnant but developed hydramnios and delivered a premature, abnormal baby who died a few hours later.

Healing of the cervix has been satisfactory in 15 patients. Scars about ½ inch long were seen in most and the external os was generally a cleanly healed transverse slit. In a few the os was patulous, admitting a fingertip—but no more than is often seen in women delivered spontaneously. The only patient with symptoms, a para-2, aged 37, had a mild degree of prolapse. Forceps had been necessary for both deliveries, and on the second occasion 4 years ago the cervix was also incised. This case is dealt with in the discussion.

Discussion

Much of the ill reputation this operation has acquired must surely have resulted from extraction of the child too early in the first stage of labour, when it was not only the cervix but also the undilated vagina and the inelastic connective tissue at the vaginal vault that acted as a barrier to descent. It is not surprising that forcible delivery of the head past these unyielding

structures resulted in gross tearing, severe haemorrhage, grave degrees of shock, and sometimes fatal injury to the foetus. Accouchement forcé in such circumstances has no place in modern obstetrics and is rightly condemned.

We are describing delivery in quite different conditions, of which three need amplification. First, with one exception, we consider it most important that the *greatest diameter of the foetal head should have already passed below the condensation of fascial tissue surrounding the cervix and upper vagina*—as judged by finding the fingers can reach high alongside the head during vaginal examination (Fig. 1). The exception is a very distensible vault such as is found occasionally in parous women. The undilated portion of vagina below the presenting part must also be elastic if laceration is to be avoided; this refers especially to its middle third, as the lower vagina and a tight perineum can easily be dealt with by episiotomy. (The presence of a soft, supple vagina is always a reassuring feature in such cases.)

Second, the *degree of dilatation* of the cervix has seemed less important to us than to Morris (1957) who has said that the risks of injury are "inversely proportional to the degree". Only two of our cases were less than half-dilated but, provided this stage was reached and all else favourable, the amount of cervix remaining made no difference either to the decision to deliver vaginally, or to its consequences when carried out. We do feel, however, that the operation is safer when the cervix is thin, as it usually is when the biparietal diameter of the head has descended below the vaginal fornices. Sometimes the undilated portion may be extremely hard and thick at its rim, but this need not deter provided the remainder is well thinned-out. That an anatomical abnormality exists in some cases is demonstrated by the "gritty" sound occasionally audible even to the onlookers as this band is divided.

Third, *disproportion* must be excluded even though it is unlikely with the head deeply engaged. A minor degree of disproportion can be an important factor in the development of inco-ordinate uterine action and therefore may well be present when incision is contemplated because of prolongation of labour. Perhaps the commonest form to escape detection is that due to an unexpectedly large child, and it is to be noted that big babies were common amongst our cases (Table II). When weighing up the circumstances prior to making a decision, the size of the child must be most carefully considered.

One allegation made against delivery before full dilatation is that it predisposes to genital prolapse. This is a claim which may be well founded if the foetal head is dragged through an undilated vault and so stretching the transverse cervical ligaments, but, if the widest diameter of the head has already passed below the vault, the act of drawing it out should not cause damage at that level. Injury to the fascial supports of the pelvic floor, and therefore prolapse in the future, may be due more to prolonged distension of these tissues by a large foetal head in the pelvis than to the method of delivery. This could account for the case of prolapse already described, as the head of a 9½ pound child occupied the pelvic cavity for some 60 hours before incision of the cervix permitted removal of the distending force by delivery. It is generally agreed that prolonged pressure of the head on a rigid perineum in the second stage of labour should be dealt with by episiotomy; in the same way it would seem simpler and safer, when the cervix is the principal cause of serious delay in the first stage, to remove the obstruction by cutting both cervix and perineum.

In any case, prolapse is a common enough sequel to normal delivery and if the patient who is likely to develop it suffers the added disadvantage of prolonged labour, whether treated by incision of the cervix or not, the likelihood of prolapse developing may well be greater. We do not feel that there is an increased liability to this complication, but a longer period of observation is required before definite conclusions can be justified.

Some relevant aspects of our conduct of prolonged labour are discussed as it is most often in these cases that we have needed to deliver before the end of the first stage. Labour so often starts slowly after a period of irregular contractions that from time to time a patient in whom there is a genuine labour abnormality is overlooked until such a late stage that treatment is prejudiced. We have tried to prevent this

by arranging that any patient whose delivery is not imminent after 24 hours in labour should be reported to a responsible member of staff so that accurate diagnosis and a policy of treatment can be determined as early as possible. Definite periods of observation, of about 4-8 hours, are usually specified and a time fixed for the next assessment. On vaginal examination we have made it our practice to note most carefully whether the conditions for safe delivery are present whatever the stage of dilatation, so that we know when this operation can be done should the need arise.

Oxytocic infusions, both in the commonly used concentration of 5 units to the litre and more recently in the very high dilutions recommended by Theobald, Kelsey and Muirhead (1956), have been occasionally successful, but this form of therapy is not in our view a substitute for incision of the cervix. The two methods are complementary, being applicable at different stages of labour. We agree with Theobald that the best results are obtained when the drip is used early, and not after the patient has suffered ineffective pains for more than 48 hours. There is a danger when employed late that excessive uterine retraction may develop, and the situation may become worse instead of better.

The timing of interference is a matter calling for much skill and judgment. Looking back over our records, earlier operation could easily have been performed, and might have been preferable in a number of patients who endured many hours of labour without obvious progress. At present we think about operative delivery much sooner than we did; our confidence in its safety may be illustrated by the case of a woman, aged 40, pregnant for the first time after 17 years of infertile marriage, whose labour began to show unfavourable features after 29 hours. She was safely delivered with forceps at three-quarters dilatation of a heathy child weighing 8 pounds 12 ounces.

O'Sullivan (1939) reported spontaneous delivery after incision of the cervix in 8 out of his 14 cases. We have not been so fortunate in that incision alone has been insufficient in all but two. In our view prompt delivery is usually to be preferred after incision.

The operation of incision of the cervix and forceps delivery is not one to be recommended for the occasional obstetrician. The decision as to whether the vaginal or abdominal route will be in the best interests of mother and child can be a close one, demanding consideration of many conflicting factors for which experience is essential. We regard it as a procedure only for those well accustomed to performing difficult vaginal delivery. We suggest that, except in the easiest cases, it is best done in an operating theatre, where good lighting and adequate assistance can be assured and facilities for any eventuality are more likely to be available than in an ordinary labour ward. There is a further advantage; at no stage of the operation is it necessary to assume that one's boats are burned and that the decision to deliver vaginally is irrevocable, for even if the cervix has been incised and forceps applied, it is still not too late, if unexpected difficulty is encountered, to turn about and perform Caesarean section. We have not in fact had to do this but we try to remember that the aim is not just to complete delivery, but to preserve, as far as this is possible, the life and health of both mother and child.

Study of published hospital reports shows that in recent years there has been a widespread increase in resort to earlier delivery though this has almost always been by Caesarean section. We think that it may not be appreciated sufficiently often that vaginal delivery is sometimes a feasible alternative. It is freely admitted that it is by no means always that a choice exists, but, when it does, vaginal delivery has much to offer.

The amount of tissue damage in a properly chosen case of incision of the cervix is trifling in comparison with that inevitable in Caesarean section. At the most two small cuts in the thin, fibrous cervix, requiring only 2 or 3 sutures each, and an ordinary episiotomy must be measured against a full-length laparotomy incision and a large wound in an important part of the uterus. In Caesarean section more blood is lost, more vital tissue planes are opened to potential infection and, most significant of all, a permanent scar is left in the uterus. Though rare, even the lower segment can rupture in a later pregnancy. It is perhaps in connexion with subsequent pregnancy that vaginal delivery

confers its greatest advantage, as Jeffcoate has shown (1949); namely, the promise of normal labour. All five patients in this report who became pregnant after a previous delivery by incision of the cervix delivered easily after quite short labours. Whilst this may also happen after a Caesarean section it cannot be presumed to be the rule. Indeed, the history of a previous Caesarean section, even though performed for a non-recurring lesion, has often been the reason for ending the next pregnancy by an elective operation, and in due course the next by yet another—sometimes with tubal ligation because of all three.

Our present ability, thanks to modern advances in chemotherapy, anaesthesia, oxytocic drugs and blood transfusion, to use the abdominal route with relative freedom and safety as a way out of most obstetric problems should not obscure the fact that the same advances also make safer older vaginal manœuvres. It is our opinion, and we believe our results show that incision of the cervix and forceps delivery late in labour in the carefully selected case is a safe, satisfactory operation.

Summary

A review is presented of delivery before full dilatation of the cervix in 44 patients in Sheffield during the years 1952–57.

The conditions required for safe delivery by the vaginal route during the first stage of labour include, deep engagement of the foetal head, full dilatation of the vaginal vault, a thin cervix, a distensible vagina, an adequate bony outlet, and no other barrier to delivery. Full dilatation of the vaginal vault may be recognized by being able to pass the fingers into the fornices beyond the biparietal diameter of the foetal head.

The main varieties of labour abnormality treated in this way, together with appropriate case histories in illustration, are described and discussed in detail. Special reference is made to relevant features in our conduct of prolonged labour.

No child was lost as a result of the procedure and no mother sustained serious injury.

The merits of timely incision of the cervix and forceps delivery under present improved conditions are discussed, and a plea is made for this operation in suitable cases in preference to Caesarean section.

Acknowledgment

Our thanks are due to Mr. L. B. Patrick, Mr. D. H. Lees, and Mr. T. Smith for permission to include three cases who were admitted under their care.

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A FATAL CASE OF RUPTURE OF UTERUS FOLLOWING EXTERNAL VERSION UNDER ANAESTHESIA WITH ASSOCIATED AFIBRINOGENAEMIA

BY

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THE following case is reported not only because this maternal death occurred with disturbing rapidity, but also because of the unusual and unexpected nature of events and the combination of interesting factors which were present.

CASE REPORT

Mrs. B.A., aged 33, was a para-4, and all pregnancies had been normal and deliveries spontaneous. The weight of the heaviest infant was 10 pounds.

In 1954 she was delivered of a stillborn infant at home. The weight of that baby, and the circumstances of this delivery, which was spontaneous, are not known.

She was admitted to the North Middlesex Hospital at the 25th week of her pregnancy because of a 2-day episode of slight vaginal blood loss. No abnormalities were found on admission. The cervix was inspected and found healthy. After a 10-day stay in hospital Mrs. A. was discharged and booked for hospital confinement. She visited the Antenatal Clinic regularly, and her general condition remained satisfactory; the blood pressure never rose to above 130/80, the urine was normal and no oedema appeared. No further blood loss *per vaginam* was reported. On a number of occasions the foetus presented as a transverse lie, but each time an external version was easily performed. In addition, at 34 weeks excess liquor was noted. An X-ray taken at that time reported that the foetus was normal and that the probable site of the placenta was in the fundus, posteriorly, to the right.

The patient was admitted at the 38th week of her pregnancy because of unstable lie and a history of ante-partum loss. On admission her general condition was satisfactory; blood pressure 120/70, urine normal. Hydramnios was present and the foetus again lay in the transverse diameter of the uterus and this time external version was unsuccessful. It was therefore decided to perform version under anaesthesia, which succeeded. Considerable difficulty was encountered, however, and a fair amount of force had to be used. No placental tissue was found in the lower segment and a high rupture was performed. Six pints of normal liquor were withdrawn and the vertex settled in the brim satisfactorily. The foetal heart was clearly heard and the condition of the patient was satisfactory.

The post-operative period was uneventful; there was no restlessness and no sedation was needed, nor did Mrs. A. complain of abdominal pain, or tenderness on palpation.

Labour did not commence until midday the following day, and there was slight drainage of normal liquor. At 5 p.m. labour was established with pains occurring every 5 minutes.

At 8.10 p.m. the patient became distressed with pains and was given 100 mg. of pethidine.

At 8.15 p.m. she felt like pushing and at 8.30 p.m. she was delivered spontaneously of a stillborn male infant weighing 8 pounds 14 ounces.

At 8.40 p.m. the placenta and membranes were delivered complete and with it occurred a loss of 20 ounces of fresh blood.

As a steady loss continued, 0·5 mg. of ergometrine was given intravenously; the same dose had been given routinely with the anterior shoulder by the intramuscular route. Blood was taken for cross-matching.

At 8.50 p.m. the patient's condition, although she had only lost about 30 ounces, suddenly deteriorated. Her blood pressure became unrecordable, her uterus was lax and loss continued. Five units of pitocin were given intravenously, the foot of the bed raised, the fundus stimulated and an intravenous transfusion of Dextraven commenced. The patient suddenly complained of inability to breathe and became uncontrollably restless. She pulled out the drip, which was transferred to the other arm. This, too, she pulled out in spite of two people restraining her. She was frothing at the mouth. Two cut down transfusions were given in the left and right saphenous veins and blood run in under pressure. She was given oxygen.

At 9.20 p.m. she lapsed into coma and died at 9.25 p.m.

The total estimated loss was 70 ounces. Total amount replaced 40 ounces (10 ounces of Dextraven and 30 ounces of blood).

None of the blood which had been lost vaginally had clotted, nor had the sample taken for cross-matching at the onset of the haemorrhage, nor a sample taken 15 minutes after death.

Post-Mortem Findings

Uterus. The organ was flabby, and in the left postero-lateral quadrant of the lower segment was a complete rupture running longitudinally, measuring 4 inches, extending into the upper segment above and the vagina below.

The parametrium and broad ligament on the left side were oedematous, and a partly clotted extravasation of blood had spread out into the parametrium, extending retroperitoneally up to the attachment of the pelvic mesocolon, into the layers of the mesocolon and on to the wall of the pelvic colon. The amount was estimated at 20 ounces.

The site of placental implantation was in the upper segment, posterior, to the right. The placenta appeared healthy. No macroscopic abnormalities were noted in heart, spleen and kidneys except generalized pallor.

Liver. It weighed 2,360 g. and was extremely pale.

Lungs. These were somewhat reduced in bulk. They were moderately congested and showed no evidence of pulmonary oedema.

Microscopical Examination

The myocardium, liver and coronary arteries were normal.

Lungs. There was no evidence of pulmonary oedema. Arteries and capillaries were dilated and markedly engorged. No evidence of mucin, hairs or epithelial squames was seen in the vessels.

Uterus. Sections at the site of rupture showed haemorrhage and infiltration with round cells, lymphocytes and polymorphs. The muscle was oedematous.

Infant's Post-mortem

No abnormalities were found. The lungs showed subpleural petechial haemorrhages, were expanded, but airless.

Biochemical Investigations

Three samples of blood were available.

(1) Five ml. taken at the onset of post-partum haemorrhage, 10 minutes after delivery.

(2) Blood passed *per vaginam* after delivery.

(3) Ten ml. of blood taken 15 minutes after death.

None of these samples had clotted 15 hours after delivery. The fibrinogen content of samples 1 and 3 could not be estimated by the usual methods. It was therefore concluded that no fibrinogen was present in the blood. A potent fibrinolysin was also found. The patient's plasma added to a normal exogenous clot produced lysis in two hours. To the patient's blood was added thrombin and fibrinogen. Lysis had occurred in the resulting clot within one hour.

Comment

Before the post-mortem findings were known it was difficult to see why a haemorrhage of not more than 70 ounces could so swiftly kill a patient who had had a normal labour. Although resuscitation was hampered in the extreme by the almost uncontrollable restlessness, more than half the blood loss had been replaced before death. The afibrinogenaemia was obvious; but was this phenomenon the ultimate explanation of the patient's precipitous death or was it a mere side effect possibly associated with amniotic fluid embolism?

The ruptured uterus found the following morning at post-mortem cast a new light on the whole question, but put yet another problem up for explanation. Why had this non-scarred uterus ruptured spontaneously in a labour which had been neither obstructed nor prolonged, and at what stage had the rupture occurred? The abnormalities during the pregnancy were: a short episode of bleeding at 25 weeks; the presence of hydramnios; an unstable lie. The significance of the stillbirth at home in 1954 could not be assessed. This might have been a "scarred" uterus after all, although no evidence thereof was found at the post-mortem. The patient had had 7 easy external versions performed during the course of her pregnancy and

one under anaesthesia one day before delivery, where considerable difficulty was encountered and a fair amount of force used. This last consideration is of importance. The blood found in the broad ligament and the retroperitoneal space had clotted and therefore must have escaped before the actual complete rupture during labour, and it had the appearance of fresh clot, showing no signs of organization. The broad ligament showed marked oedema which was unlikely to have formed in the short space of one hour. Some time before death, blood, therefore, must have slowly leaked into the layers of the parametrium; so slowly that no clinical signs of reduced blood volume were produced. Infiltration with round cells, lymphocytes and polymorphs round the area of the rupture indicated some reactive process, suggestive again of some event occurring before death.

Six pints of normal liquor were withdrawn at the time of artificial rupture of membranes, and the liquor which escaped later was at no time blood-stained. In fact, there was no haemorrhage until the second stage was over. It seems, therefore, certain, that at some time before delivery a partial rupture had occurred and blood had leaked out into the surrounding tissues. This must have occurred during the version under anaesthesia the day before, when the uterus, already stretched by excess liquor, and possibly scarred by a previous accident, received the trauma necessary to cause a partial rent in its wall. A short, vigorous labour tore the last remaining fibres, thereby making the rupture complete. Although the laceration of the lower segment and the blood loss could easily account for extreme shock, it was difficult to accept that they had caused death in under one hour.

Conditions for amniotic fluid embolism were almost completely fulfilled: large venous sinuses widely patent to receive the liquor amnii. An extensive search was therefore made in the lungs for evidence of such embolism. The gross appearance of the lungs did not suggest it. The sections admittedly showed dilated and congested vessels but no pulmonary oedema, vernix, lanugo hair, meconium (mucin), or epithelial squames. Multiple sections were stained with Best's mucicarmine but shed no further light.

In conclusion it could, therefore, be said that in all probability a partial rent in the uterus, possibly in a previously weakened area, had been caused by the external version. This ruptured during labour and death occurred within one hour from the combined traumatic effects of the rupture and the ensuing blood loss, probably aggravated by afibrinogenaemia.

Discussion

In series of uterine rupture, reported over the past 35 years, the incidence of spontaneous, non-Caesarean rupture varied between 5 and 30 per cent, with an average mortality of 56 per cent.

Chassar Moir (1956) lists the aetiology of spontaneous rupture, apart from the scarred uterus (Caesarean section, myomectomy, etc.): adenomyosis, uterine maldevelopment, obstructed labour, multiparity, and unrecognized bruising and lacerations during previous labour. Additional factors, as given by authors of large series, are: excessive proliferation of chorionic epithelium, or deficiency of uterine decidua, prolonged labour, abruptio placentae and oxytocics. In none of the large series and cases reported, however, nor in current textbooks studied, is external version mentioned as a predisposing or causative factor.

Since 1933 only 6 authors have reported large series of external version under anaesthesia, and their articles include very little about maternal mishaps following this procedure. Only Freeth and MacVine (1951) reported a case of maternal trauma, in fact a ruptured uterus in a woman of 40, of unknown parity, necessitating laparotomy and Caesarean section. The foetus presumably died, but the uterus was sutured, and the patient recovered.

White and Flew (1933) noted vaginal bleeding in 6 cases out of 92 anaesthetized, but did not record maternal trouble.

Wrigley (1934) for foetal reasons condemned version under anaesthesia after surveying 76 cases.

Newell (1941) turned 48 breeches, with no maternal mortality.

Odell (1946) described a version under anaesthesia causing placental separation and such a degree of shock that a Caesarean

hysterectomy had to be performed. The patient was severely hypertensive, nowadays considered a strong contra-indication to version.

Peel and Clayton (1948) published the largest series found. They put in a strong plea for version under anaesthesia in cases in which version has otherwise failed, and maintained that the operation is not unduly dangerous, but did not mention maternal mishaps, and confined themselves to discussing the foetal risks.

Freeth and MacVine (1951), writing about the results of 214 versions without maternal mortality, consider that multiple pregnancy, suspected placenta praevia, toxaemia, marked hypertension and previous classical Caesarean section are contra-indications for version under anaesthesia.

Fell (1953) surveyed 102 versions performed in the Middlesex Hospital. Again no maternal accidents occurred. He discussed the maternal risks, saying that cases of rupture had been reported; "this is a very rare happening and the possibility seldom needs consideration".

One has to go back as far as 1933 to find a causative relation between version, ruptured uterus and maternal death, when McCullagh collected 3 fatal cases, the cause of rupture, however, being the malpresentation caused by the version, and not the trauma to the uterus.

The occurrence of afibrinogenaemia in obstetric practice is now well recognized and the number of cases reported increases every week. It is interesting to see that this phenomenon was noticed as far back as 1769 by Morgagni, who found fluidity of blood in a victim of murder. John Hunter in 1794 noticed post-mortem incoagulability in cases of sudden death produced by many kinds of fits, anger, lightning, etc. (both quoted by Mole, 1948).

Yudin, in 1936, made practical use of observations on this subject by storing the blood bank of the Shleforsovsky Institute in Moscow with blood taken from victims of street accidents and other cases of sudden death in otherwise relatively healthy persons. Blood collected aseptically, was found to clot initially but liquefied within 1½ hours. He made the interesting observation, "That it would appear that in a shocked patient fibrinolysis begins while the patient is still alive".

In 1948 Mole investigated the blood of 61 routine autopsies. He found that in a number of cases where death had occurred suddenly, the blood was coagulated only during a brief period after death. In 90 per cent of those cases a fibrinolysin was demonstrated.

Most of the obstetric cases now reported are associated with severe accidental haemorrhage, post-partum haemorrhage, retention of a dead foetus *in utero* (dead-foetus syndrome) and amniotic fluid embolism. Hypofibrinogenaemia has been noted to occur in a 19-weeks abortion (Norburn, 1957).

Phillips, Montgomery and Taylor (1957) reported 8 cases, one occurring in association with a ruptured uterus, showing many similarities with the case presented.

Hodgkinson *et al.* (1955) recognize a dual symptomatology during the fibrinogen-fibrin conversion process. The initial impact causes "obstetric shock" from massive intravascular fibrin embolism; the secondary effect may be the haemorrhage which ensues.

In our present state of incomplete knowledge of the phenomenon of afibrinogenaemia and its causation, there can be no certainty about its part played in Mrs. A.'s case. She may have succumbed to the overwhelming effect of intravascular embolism; the partly replaced blood loss, and the effect of rupture were aggravating, albeit initiating, factors. On the other hand, the fatal outcome may have been the result of rupture and blood loss, and the afibrinogenaemia a side-effect or agonal sign, as Yudin described, happening in severely shocked patients while still alive.

Searching for the "avoidable factor" in this maternal death, one cannot escape the feeling that Mrs. A.'s life might have been saved, if it had been possible to replace the lost blood more fully and more instantaneously.

Summary

(1) A case is presented of rupture of the uterus with fatal outcome, associated with afibrinogenaemia.

(2) Arguments are put forward that partial rupture occurred during an external version under anaesthesia the day before delivery.

(3) The three aspects of the case, rupture, maternal trauma after version under anaesthesia, and afibrinogenaemia, are briefly discussed in relation to published series and cases and current views in the literature.

ACKNOWLEDGMENT

I wish to thank Mr. K. A. Hudson for his permission to publish this case.

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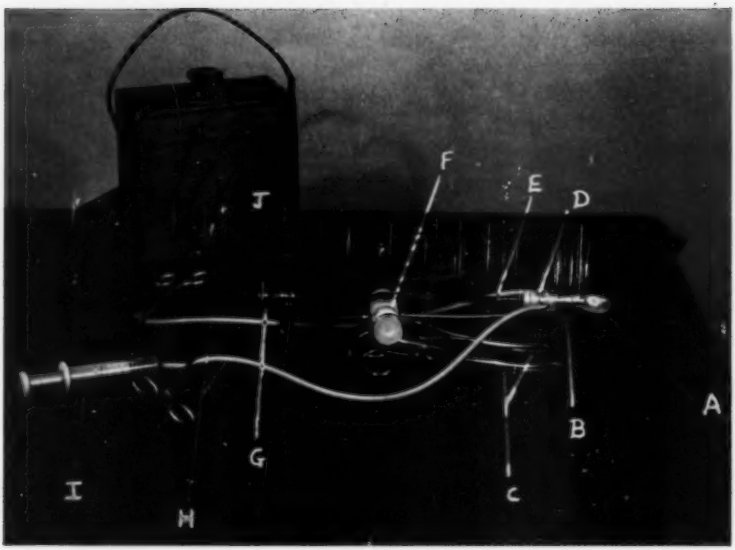

FIG. 1

Hysteroscope. A—transparent rubber balloon; B—stem of carrier, which lies in the cervical canal; C—the two volsellum forceps, fixed to F; D—the head of the carrier which abuts on the cervix; E—marker; F—handle of carrier; G—straight cystoscope; H—water inlet and outlet tubes; I—20 ml. syringe; J—battery.

A HYSTEROSCOPE

BY

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ONE of the few body cavities not explored visually is the uterus. For such examination a hysteroscope has been designed, independently of that described by Norment (1952, 1956). For its development post-hysterectomy uterine specimens were at first used. Later it was used *in vivo*.

The principle of the apparatus is essentially to produce conditions similar to cystoscopy in which the bladder is filled with water. As the uterine cavity is unable to be filled with fluid without the danger of leakage into the peritoneal cavity, a transparent balloon is placed in the uterine cavity and distended with water. The balloon takes the shape of the uterine wall and the viewing is done through this transparent "window" with a special cystoscope. Furthermore, the balloon eradicates the problem of blood, debris, etc., clouding the lens and so obscuring the view.

The hysteroscope (see Fig. 1) consists of a straight cystoscope (G), having a 6 mm. diameter sheath, and a transparent rubber balloon (A) fixed on to a perspex carrier (D), which has a handle (F).

The carrier has a water inlet and water outlet tube (H), to serve the balloon. The cystoscope is passed through a water-tight hole in the carrier to enter the cavity of the balloon. The apparatus is now ready for use. The red marker (E) on the cystoscope sheath is movable and is set to the length of the uterine cavity, after measurement with a sound.

METHOD OF USE

The patient under general anaesthesia is prepared as for a dilatation and curettage operation. Two volsellum forceps are applied to the cervix, and the cervical canal dilated up to the No. 7 gauge dilator. A rubber catheter is inserted and the uterine cavity gently syringed with 5–10 ml. of sterile normal saline. (This helps to remove any free blood and debris, and dilutes the acidity of the uterine secretions which may cause clouding of the balloon.)

The balloon attached to its carrier and riding on the cystoscope is inserted into the uterine cavity, the carrier fitting squarely up against the cervix. To maintain the hysteroscope in position the handles of the volsellum forceps are fixed to the handle of the carrier by means of screw-in caps. (The cystoscope may then be rotated in any direction.) The balloon is expanded using normal saline. Examination of the uterine cavity is now carried out. Interpretation of what is seen comes with experience, and does not present any difficulty.

In order to expand the balloon without retaining an air bubble the following procedure is adopted. First the outlet tube is closed by a small artery forceps. The balloon is expanded with about 5–8 ml. saline, using a 20 ml. syringe, and the inlet tube then clamped off. Now the water is allowed to run out by opening the outlet tube. The elasticity of the balloon will force out the air bubble. The balloon is filled once again, using 10–15 ml. water, whilst keeping the outlet tube closed, and it is now ready for use.

I am much indebted to Mr. S. J. Meir, Radiotherapy Department, for his patience and skill in making the parts for this hysteroscope; Messrs. Veedip Ltd., Slough, Bucks., for making the balloons for me; Mr. M. D. Keates for his continual encouragement; Mr. F. W. Duthie and Mr. L. M. Edwards for permission and help with the trials.

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Obituary

FRANK HAMILTON LACEY

T.D., M.D., F.R.C.O.G.

It is twelve years since F. H. Lacey worked among his colleagues and friends as a busy consultant in Manchester and retired to his farm in Sussex. His death on 11th April, 1958, aged 78 at his home Langton Farm, Balcombe, recalls memories of a delightful personality enhanced by the touch of Irish in his blood. He was born on 2nd May, 1879, in Dublin, the second son of Dr. Thomas Samuel Lacey, later in general practice near Oldham, and was educated at Manchester Grammar School and Manchester University, graduating M.B., Ch.B. in 1906 and proceeding to the M.D. in 1912. He was elected one of the Foundation Fellows when the Royal College of Obstetricians and Gynaecologists was founded in 1929.

After holding house-surgeons posts at St. Mary's Hospital, Manchester, he succeeded Fletcher Shaw in 1908 as senior resident officer, a post which he held for four years, and which provided clinical training in obstetrics and gynaecology of unique value. His active connexion with St. Mary's—as registrar, assistant and full honorary surgeon—continued until his retirement in 1946, being broken only for four years by the first world war, in which he served in Gallipoli with the R.A.S.C. Territorials, and later in France with the R.A.M.C., retiring with the rank of major, and subsequently being awarded the Territorial Decoration.

He was a Clinical Lecturer in obstetrics and gynaecology in the University of Manchester. He acted as a vice-president of the Section of Obstetrics and Gynaecology of the British Medical Association at its Annual Meeting in Manchester, 1929.

He held the post of gynaecologist to two large municipal hospitals in Manchester at different periods until his retirement, and was for many years honorary gynaecologist to the Christie Hospital for Cancer.

Lacey was most conscientious in carrying out his work in the hospitals, assiduous in attendance in out-patient clinics, wards and operating theatres and in bedside teaching of medical students. He lectured to midwives for the Central Midwives Board and was keenly interested in their training. He was an examiner for the C.M.B. and for many years supervisor of examinations at the Manchester centre.

At meetings of the North of England Obstetrical and Gynaecological Society he took his full share in discussions and was President in 1932. In the usual dinners after these meetings Lacey was in his element as a raconteur and wit.

He was perhaps at his best at meetings of the G.V.S. at home and abroad, and he enjoyed partaking in the criticizing of the displays organized by the hosts of the meetings, and entering with zest into the conviviality characteristic of the Society.

Of the two branches of our specialty it may be said that Lacey had a flair for obstetrics and, when in 1912 the writer of this notice came under his tutelage and the incidence in the hospital of Caesarean section for contracted pelvis was 20 cases per annum in contrast with 65 cases in 1948, his manipulative skill in difficult deliveries *per vias naturales* was remarkable for its success.

A modest man he made no claim to academic distinction and his writings were few, neverthe-

FRANK HAMILTON LACEY

less, his contribution to this journal in 1921, "Results of vaginal operations for prolapse by the Manchester School", went far to establish the reputation which the Manchester operation of colporrhaphy has gained.

Lacey's joy in social gatherings has been alluded to already. Although almost blind and with his health in a precarious state, his pluck and a desire to pay tribute to his old friend and colleague enabled him with his wife's devoted care to come up from Sussex to the R.C.O.G. house for Fletcher Shaw's 80th birthday party on 10th April, 1958, and there he was his usual genial self, chatty and humorous, dwelling on memories of the past. Of the many former happy meetings with his colleagues and friends then present, this brief one, during the few remaining hours of his life, may surely be reckoned one of the happiest.

Frank Lacey married Miss Evelyn Rudge in 1915 during the first world war. She survives him with two sons, the younger of whom John, a regular soldier, married a niece of W. Blair-Bell, and one daughter, to all of whom we extend our sympathy.

JOHN BRIDE.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of the Council was held in the College House, on Saturday, 26th July, 1958, with the President, Professor A. M. Claye, in the Chair.

The following Officers were re-elected:

President

Andrew M. Claye, Esq., M.D., F.R.C.S., P.R.C.O.G.

Honorary Treasurer

Arthur C. H. Bell, Esq., M.B., B.S., F.R.C.S., Hon.M.M.S.A., F.R.C.O.G.

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Ian M. Jackson, Esq., M.B., B.Ch., F.R.C.S., F.R.C.O.G.

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R. Alan Brews, Esq., M.D., F.R.C.S., F.R.C.O.G.

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John N. Chesterman, Esq., F.R.C.S.E., F.R.C.O.G.

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Honorary Treasurer, New Zealand Regional Council

A. M. Rutherford, Esq., M.B., Ch.B., M.R.C.O.G.

Honorary Treasurer, South African Regional Council

F. N. Charnock, Esq., M.B., Ch.B., M.R.C.O.G.

The following Officers were elected:

Vice-Presidents

G. F. Gibberd, Esq., M.B., M.S., F.R.C.S., F.R.C.O.G.

S. W. Maslen-Jones, Esq., M.B., M.S., F.R.C.S., F.R.C.O.G.

The following candidates have been elected to the **Membership:**

Prabhavathy Aiman.
Prasannatissa Harischandra Amarasinghe.
David Thomas Cecil Barber.
Carl Theodore Herzil Barrett.
Walter Philip Bonnici.
John Breeze.
John Michael Brudenell.
Donald Pui-Chee Chan.
Hermanus Johannes Hendrik Claassens.
Cecil John Tainton Craig.
Dilip Ranjan Das.
Robert Morrison Davie.
Richard Francis Drake.
Graeme Ross Duncan.
George Herbert Ellidge.
Wellege Hemachandra Fernando.
Leonard Henry Fienberg.
James MacDougal Graham Harley.
Denys Heginbotham.
James Bleakley Hemsley.
Alice Hsiang-Lien Hsu.
Peter John Huntingford.
Sylvia Ray Ingold.
Katherine Isobel Jack.
Robert Douglas Johnstone.
Ellis William Parry Jones.
Anthony John Keane.
Arthur Charles Keast.
Denis Malcolm Davies King.
Sybil Vera Kinley.
Daphne Rae Lowe.
John McGlone.
Sheila Malhotra.
Gouri Sankar Mandal.
Denis Thorpe Mathews.
Charu Chandra Mitra.
Diana Montgomery.
William Peter Lochrane Morrison.
Alexander Desmond Muirhead.
Salvino Muscat.
Sapugahawattege Henry Pijadasa Nanayakkara.
Isabella Ross Napier.
Hannah June Pash.
John Herbert Peters.
David Walter Pfanner.
Carmen Mary Rant.
Denzil Mervyn Reader.
Walter Joseph Cyril Rebello.
John St. George.
Ajit Kumar Sarkar.
Peter Cameron Stichbury.
Jean Orr Struthers.
William Moss Elvery Tweed.
Radha Naravan Udipi.
Thiagarajah Visvanathan.
Alistair William Goold Weir.
Dorothy June Whitney.
William Geoffrey Wicks.
Balasubramaniam Yoganathan.

REPORTS OF SOCIETIES

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

JANUARY 1958

The Annual General Meeting of the North of England Obstetrical and Gynaecological Society was held in Manchester on 17th January, 1958. The following were elected officers for 1958:

President—Dr. E. A. Gerrard.

Vice-Presidents—Miss M. Evans (Manchester), Mr. C. J. K. Hamilton (Liverpool), Mr. G. W. Theobald (Leeds), Professor C. S. Russell (Sheffield), Mr. F. J. Burke (Newcastle).

Hon. Treasurer—Mr. C. H. Walsh.

Hon. General Secretary—Miss E. Mills.

Hon. Reporting Secretary—Miss U. M. Lister.

Dr. Gerrard took over the Chair from the retiring President, Mr. F. Stabler.

Mr. R. T. Sears reported a case of

POST-PARTUM JAUNDICE WITH HYPOTENSION AND ANURIA

The patient was aged 28 years, a gravida-5, her previous pregnancies having been normal, and the antenatal period, which was supervised by her own doctor, had been uneventful apart from some malaise two weeks prior to delivery.

The membranes ruptured spontaneously 1 week after the expected date of delivery, and labour commenced 48 hours later. She was admitted to hospital early on 25th July, 1956, on account of meconium-staining in the liquor, and after a labour lasting 36 hours was delivered at 2 a.m. next day. The post-partum loss was 2 ounces. The child was stillborn, foetal death being attributed to the cord tightly round the neck.

The general condition of the patient on admission to hospital and her blood pressure had been good, and the only abnormality noted in the 24 hours prior to delivery was a slight rise in temperature. This was attributed to urinary or intra-uterine infection, but the urine and high vaginal swab were subsequently shown to be sterile.

During the first day after her delivery, the patient seemed well, her general appearance satisfactory, and it was because of this that two important factors were overlooked. The first was that immediately post-partum her blood pressure was 80/50 mm. Hg, and the second that no urine was passed on the first day of the puerperium. It was only when moderate jaundice was found next morning, 30 hours after delivery, that she was seen to be very ill, the pulse rate being 110 per minute and blood pressure 68/40 mm. Hg. No other abnormality could be found, her haemoglobin was 93 per cent, and white cell count 30,600 per ml. The plasma albumin was lowered, alkaline phosphatase slightly raised, and thymol turbidity normal.

Treatment with 400 mg. cortisone and 10 per cent glucose solution intravenously resulted in a rise in blood pressure, but only 9 ounces of urine had been passed by the 4th day. Jaundice deepened, petechial haemorrhages appeared, and the temperature fell below normal, so that the prognosis seemed hopeless.

On the 5th day there was some improvement, but the non-protein nitrogen had reached 158 mg. per cent and serum potassium 25·8 mg. per cent, and there seemed danger from renal failure. She was treated by Bull's regime, maintenance of fluid and electrolyte balance was not difficult, and gradually urinary output improved.

The exact diagnosis in this case is still uncertain. There was no evidence of infection, and there seems little doubt that jaundice was due to liver damage rather than haemolysis, the history of malaise suggesting infective hepatitis. Hypotension is a well-recognized accompaniment of severe liver damage. In this case it was felt that adrenocortical failure might be responsible for the hypotension, renal failure being secondary to the low blood pressure, and that the use of cortisone or hydrocortisone was vital in the treatment.

Discussion

Dr. C. J. Dewhurst agreed that it was impossible to exclude adrenocortical failure. Recently he had seen a patient who became jaundiced 12 hours after delivery, oliguria developed but there was no hypotension.

Mr. D. Keith had known a similar case with jaundice and oliguria following a blood transfusion and small accidental ante-partum haemorrhage. There was prolonged hypotension, and a further blood transfusion caused a rapid rise in pulse rate, a satisfactory response being obtained with plasma transfusion.

Dr. F. M. Parsons had found that the majority of patients with acute renal failure also developed jaundice within the first 48 hours. Though the combination of these two conditions is common, the reason is not yet known.

Dr. Sears, in reply, mentioned another case who collapsed after normal delivery. Cortisone was given for 14 days, but jaundice was evident for the first 3 to 4 days.

Dr. F. M. Parsons and Dr. B. H. McCracken read a paper on

THE ARTIFICIAL KIDNEY AND THE TREATMENT OF ACUTE RENAL FAILURE

(This article appears on page 631 of this issue)

Discussion

The President found the paper most instructive and stimulating. This type of patient has always been most worrying, but now Leeds is pointing the way to better treatment and results.

Dr. R. Newton tried to assess the need for an artificial kidney on the west of the Pennines. In the Manchester region there had been in 25,000 deliveries 5 deaths in which renal failure played a part, and only 3 of these patients might have benefited from the artificial kidney.

Mr. F. Stabler congratulated Dr. Parsons and Dr. McCracken. It had been said that patients should be sent early. Did this mean all with anuria, or those failing to respond to diet restrictions?

Dr. D. Keith asked about the practice of maintaining a high haemoglobin level, by transfusion if necessary.

Dr. F. Da Cunha mentioned a case of anuria following concealed accidental ante-partum haemorrhage. Despite Bull's regime the blood urea rose to 400 mg. per cent on the 9th day, and she was transferred over icy roads to Leeds. He asked about intravenous catheterization and ion exchange resins.

Mr. T. B. FitzGerald sought further information about the use of vitamins and the persisting renal damage.

Mr. H. H. Francis enquired about a suitable dietary regime instead of Bull's diet. In the original method vomitus was returned, but may this not infect the alimentary canal? He also asked if there was any change in the blood chemistry more lethal than others.

Miss K. Liebert asked if there was a limit to the number of dialyses.

Dr. McCracken spoke in reply.

In France it had been estimated that there should be 1 machine for 10 million of the population, and on this estimation Britain would need 5, but geography played a part. At the moment the load on the machine was sufficient, but probably not all cases were sent. In general, blood urea figures were a useful guide as to when to send the patient, but 48 hours preparation were needed before dialysis. A blood urea nitrogen level of 200 mg. per cent required dialysis.

Blood transfusion should be avoided if possible owing to the high potassium content and the breaking-down of aging cells. At the time of the dialysis the 2 pints of blood needed to fill the machine could be transfused.

Complications such as infection occurred with venous catheterization, and post mortem a surprising amount of thrombosis was found. It was best avoided.

Usually when potassium intoxication arose there was a need for dialysis, and if ion exchange resins had been given, the potassium loss went on and levels might become too low.

Vitamins were given on general principles more than from exact knowledge.

These cases did not occur in sufficient numbers and the time was as yet short for a definite prognosis. Six months later renal function was usually about 50 per cent. Impairment did not seem to be progressive.

There were hazards in the old Bull regime with regard to infection, and intake was confined to oral 20 to 25 per cent glucose solution with flavouring.

The various elements in the blood chemistry were intriguing. Potassium if too high was lethal and the carbon dioxide combining power ran parallel to the clinical deterioration. There was no limit to the number of dialyses that could be undertaken until the blood vessels ran out.

NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

FEBRUARY 1958

A meeting of the North of England Obstetrical and Gynaecological Society was held in Liverpool on 21st February, 1958. The President, Dr. E. A. Gerrard, was in the chair.

Dr. M. Goodman recorded

A CASE OF RETICULUM CELL SARCOMA IN PREGNANCY

(This article appears on page 641 of this issue)

Discussion

The President commented on the rareness of this condition, of which he had no personal knowledge.

Dr. S. Bender raised the question of the management of a pregnancy in the presence of malignancy. Usually the malignancy was a carcinoma of the breast. Dr. Bender had had one such patient in whom two pregnancies had been terminated, but the third continued. Pregnancy does not expedite the growth or the recurrence and in the past we have been too severe in terminating pregnancies.

Professor C. S. Russell, Mr. C. J. Dewhurst and Dr. D. H. Blakey presented a paper on

DELIVERY BEFORE FULL DILATATION WITH SPECIAL REFERENCE TO INCISION OF THE CERVIX

(This article appears on page 644 of this issue)

Introduction by Professor C. S. Russell

Nearly 20 years ago, when I was in Oxford working as assistant to Professor Moir I was looking after a woman who was trying to have twins; her labour was prolonged, she was distressed, and needed to be delivered. I recommended Caesarean section, but Professor Moir advised me to incise the cervix and use forceps, which I did. Now if my memory doesn't serve me false the cervix

could not have been more than about two to three fingers dilated, yet the delivery was simplicity itself. I made a mistake in the conduct of the delivery of the second twin, but that is quite another story, and I needn't bother you with it today. Other cases were similarly and successfully treated. When I went to Manchester at the beginning of 1947, I continued to practise what I had learned, and to incise the cervix and deliver by forceps when I thought the occasion was suitable; and I passed my knowledge on to others, including Dewhurst and Blakey who now work with me in Sheffield. Recently, we reviewed quite a number of these Manchester cases because we wanted to be reminded in detail of the sort of work we did then. Many cases were successfully treated, but as you know, Mr. President, that was the time of the high birth rate, and many neglected cases were coming to St. Mary's; though the results of cervical incision and forceps delivery were on the whole pretty good, on one or two occasions Caesarean section should have been preferred. In Sheffield, this policy has continued, and I and my assistants have done this operation on a number of occasions during the last 7 years; it is this more recent experience that we wish to bring to this Society. We do this, not because there is anything new or original about incision of cervix and forceps delivery, indeed this Society discussed this some 7 years ago, but because we think that for carefully chosen cases this is much to be preferred to Caesarean section and because we think there are some who need to be convinced that what we believe to be true really is true. So much for the background; Mr. Blakey, who has worked with me in Sheffield ever since 1950, is going to present our paper.

Discussion

The President felt sure that Members of the Society would wish to congratulate the Sheffield team. This procedure had a definite place, but it must be stressed that the four criteria are essential, and it is suitable only in the hands of experienced people.

Mr. H. V. Corbett had reported a number of cases to the Society 7 years ago, and Mr. J. W. Hunter a series 30 years ago. In 10 years at the Liverpool Maternity Hospital there had been 10 cases of division of the cervix with a stillbirth rate of 40 per 1,000 live births. In O'Sullivan's series the average length of labour was 100 hours, and the stillbirth rate was much higher. This is an operation for the professional. It has a shady past and an uncertain future.

Mr. T. F. Redman also observed the criteria expressed by Professor Russell. He thought that in many cases it did not much matter if the cervix was stretched, tore spontaneously or was cut. Even after suturing the union is often poor.

Mr. P. Malpas was opposed to the suggestion that there was one practice for the Obstetrician and another for the General Practitioner. He thought he knew more about the shady past than most. The rule about dilatation of the cervix must never be broken. No mention had been made about why the cervix failed to dilate. There were 4 reasons: a posterior position, too big a baby, a small pelvis, and rarely the cervix fits as a cap over the head and may be seen at the vulva. In these 2 or 3 cases incision is justifiable.

Mr. W. Hunter supported Mr. Malpas, and thought indiscriminate incision a retrograde step. Cases where one is tempted to cut the cervix are usually cases of cephalopelvic disproportion or inco-ordinate uterine action. Mr. Hunter felt unhappy about the number of cases, and where the occiput is posterior, manual rotation of the head is often followed by dilatation of the cervix.

Mr. T. B. FitzGerald defended the procedure and thought these 44 cases had been treated with admirable discrimination.

Professor T. N. A. Jeffcoate thought there was a midway position. Cervicotomy is not a drastic procedure, and in carefully chosen cases there are few complications. It is like the challenge of vaginal hysterectomy, and could easily be applied to unsuitable cases, but in a few it was admirable. He had known 16 patients who after cervicotomy had returned for an easy delivery in the next pregnancy.

Mr. L. Snaith came down on the Sheffield side, but thought that caudal anaesthesia should be employed to assist cervical dilatation.

Mr. H. H. Francis enquired about the use of cervicotomy in breech delivery where the head was trapped by incomplete cervical dilatation.

Mr. C. J. Dewhurst replied.

Healing was not usually perfect. He was interested in Professor Jeffcoate's cases and their subsequent easy deliveries. It had not been possible to find how many of the Sheffield series were infertile. The cases for cervicotomy must be carefully selected and evaluated, and in none of the Sheffield series had there been a previous cervical amputation. In breech presentations he thought there might be a small place for cervicotomy.

HOSPITAL REPORTS

BY

JOHN S. TOMKINSON, M.B., F.R.C.S., M.R.C.O.G.

THE REPORT FROM THE OBSTETRIC HOSPITAL OF UNIVERSITY COLLEGE HOSPITAL, LONDON, FOR 1955

THIS interesting report is an accurate reflection of the high standard of work attained in obstetrics and gynaecology at University College Hospital, London. It consists of an Introduction (describing the layout of the department), a Critical Review (summarizing and yet expanding the details of the tables of the report), a Statistical Review of the year's work, mention of one obstetric death and one case of special interest, then follows the tables as recommended by the Royal College of Obstetricians and Gynaecologists. A Paediatric Report and a Gynaecological Report complete the account of the Obstetric Hospital.

In 1955, 31 gynaecological and 55 maternity beds were available, with 5 unclassified beds and a premature baby unit of 12 cots. An isolation unit consisted of 5 single rooms and an open ward of 5 beds. The labour ward suite had been reconstructed and was on one floor. Regular conferences for the discussion of research, perinatal mortality, and obstetric problems were held.

A total of 1,416 women were delivered during the year, 843 being primiparae. One maternal death occurred from aplastic anaemia thought due to chloramphenicol. The stillbirth rate was 19·84 per 1,000 live births and the neonatal mortality 14·1 per 1,000 live births. Thirty-seven patients were delivered on the hospital district. The Flying Squad was called out 22 times, in 12 instances for post-partum haemorrhage and 6 times for post-partum haemorrhage and retained placenta.

The table of Associated Diseases includes 30 cases of pulmonary tuberculosis, many being referred from the chest clinic of the parent hospital. The 4 cases of diabetes mellitus were admitted about the 34th week of pregnancy and allowed to go to term. Ten cases of prolapsed disc were admitted, this high incidence occurring because all cases of pregnancy backache were investigated by one clinician.

Good antenatal supervision with particular reference to weight gain is said to account for the low incidence of pre-eclampsia, this being 2·9 per cent of all deliveries.

A labour lasting 48 hours or more occurred 22 times (an incidence of 5 per cent). A prophylactic course of penicillin and streptomycin was given after labour had lasted 24 hours. A pitocin drip infusion was given to suitable patients and recordings of the uterine contractions made with the tocograph and of the foetal heart with the phonocardiograph; a grant from the Nuffield Foundation enabled a research team to study problems arising from such cases.

All patients being delivered received ergometrine 0·5 mg. with hyaluronidase 1,000 units I.M. with the crowning of the head. This procedure resulted in a post-partum haemorrhage rate of 3·8 per cent and a manual removal of the placenta incidence of 1·9 per cent of all deliveries. The Caesarean section rate was 2·8 per cent (and a post-operative pyrexia occurred in 26·8 per cent). The overall forceps rate was 5·7 per cent.

THE REGISTRARS' REPORT OF THE LIVERPOOL MATERNITY HOSPITAL FOR THE YEAR ENDING 31ST DECEMBER, 1955

THIS report includes an introductory general statement, a ten-year comparative table of statistics, the tables set out in the form recommended by the Standard Maternity Hospital Report Committee of the Royal College, details of the Liverpool Area Flying Squad cases and a Paediatric section. The Liverpool Maternity Hospital and its Southport Annexe has 125 in-patient beds; the total number of deliveries was 2,726 (of which 203 were unbooked cases) and the average stay per patient was 12·4 days. Five maternal deaths occurred, 4 of them in booked cases. The Districts Domiciliary Service attended 986 patients in their own homes, delivering 841 women and transferring 90 to hospital before or during labour; no maternal deaths occurred in this service, with 10 stillborn infants and 3 neonatal deaths.

The table of comparative statistics from 1946 to 1955 inclusive shows that the stillbirth rate of 2·6 per cent in 1955 was the lowest recorded during the decade, the neonatal death rate of 1·8 per cent was about average, as was also the maternal death rate and the forceps delivery rate of 11·6 per cent (with a foetal mortality of 2·8 per cent). Fewer Caesarean sections were performed than in any other year of the decade (incidence of 8·5 per cent). From having no foetal deaths due to uncomplicated breech deliveries in 1954, the foetal death rate from this cause in 1955 rose to 6·66 per cent, the worst figures of the ten years.

The incidence of pre-eclampsia, essential hypertension and chronic nephritis was 9·3 per cent of all deliveries and 3 cases of eclampsia were admitted. Of the 16 cases of placenta praevia, 12 were treated by

lower segment Caesarean section and 4 were delivered *per vaginam*.

In the management of persistent posterior position and transverse arrest of the occiput, Kielland's forceps rotation was used in more than one-third of the cases, more often than manual rotation. For uncomplicated breech deliveries, forceps to the aftercoming head were used in all cases but one.

A surgical induction of labour was performed in 357 patients (12·3 per cent of patients delivered); by far the commonest indication was postmaturity (256 cases) followed by pre-eclampsia or hypertension (80 cases).

A Caesarean section was carried out in 231 patients, the commonest indications being contracted pelvis (70), repeat Caesarean section (29) and pre-eclampsia (30). All but 4 were lower uterine segment sections.

The staff of the hospital is to be congratulated on a successful year's work. This report will repay a close study.

THE CLINICAL REPORTS OF THE MATERNITY DEPARTMENTS OF OUR LADY OF LOURDES HOSPITAL, DROGHEDA, AND THE WATERFORD MATERNITY HOSPITAL, AIRMOUNT, WATERFORD, FOR 1956

THE reports of these two hospitals in Eire are combined in one booklet. The tables recommended by the Standard Maternity Hospital Report Committee of the Royal College of Obstetricians and Gynaecologists are followed to some extent, being supplemented by useful summaries which comment on the results and explain some of the procedures.

(1) At Drogheda, 1,326 viable infants were delivered with a foetal loss of 4·5 per cent, a slight improvement on the preceding year. Two maternal deaths were recorded; one a case of chorionepithelioma admitted 9 weeks after a normal delivery because of vaginal bleeding. A piece of ? placental tissue was removed digitally under general anaesthesia and was not sent for histology, but a month later she was re-admitted and further tissue removed which was reported as choriocarcinoma. A chest X-ray showed many secondary deposits 4 months after delivery. A total hysterectomy with removal of adnexae was performed and she subsequently died (wrong date given). The other maternal death occurred in a para-1, aged 36, who had a blood pressure of 260/160 and some albuminuria at the 16th week of pregnancy and who died 3 months after a spontaneous abortion at the 27th week from renal failure due to malignant hypertension. In this account, again, wrong dates are given. Symphysiotomy was performed in 28 patients, "there were no serious complications of the operation and follow up has fully justified its use". The forceps rate was 5·9 per cent and the Caesarean section rate 1·2 per cent.

One interesting case is described of intraperitoneal haemorrhage due to a small vessel bleeding through a shallow laceration one inch in length in the posterior wall of the broad ligament, following very easy forceps delivery. She was very shocked and nearly dead when an exploratory puncture of the abdominal cavity revealed blood; she was transfused with 6 pints of blood and a laparotomy performed showing about 5 pints of blood in the abdominal cavity. She made an uneventful recovery.

(2) At Waterford 30 maternity and 2 isolation beds were available in 1956 and 601 patients were delivered. Much of the hospital's work was concerned with unbooked abnormal cases, for 63·2 per cent of the patients delivered were abnormal and 57·2 per cent were unbooked. Taking as a standard for toxaemia a combination of any two of the following—a blood pressure of 140/90 or over, albuminuria and oedema—then 23·3 per cent of the patients had toxaemia. The total foetal loss (including pre-viables) was 5·4 per cent, a fall of 1·1 per cent compared with 1955, the stillbirth rate 3·0 per cent, the forceps rate 9·5 per cent and the Caesarean section rate 2·1 per cent.

THE CLINICAL REPORT OF THE CRESSWELL MATERNITY HOSPITAL, DUMFRIES, FOR 1953

A TOTAL of 1,474 patients were delivered in this hospital during 1953 and, of these, 269 patients were unbooked cases. No maternal death occurred. Ten cases of eclampsia are recorded, in 2 instances the method of treatment is not mentioned and in the remaining 8 patients Tribrom. Ethanol per rectum was administered; no infants were stillborn and only one died neonatally.

Forty uncomplicated breech deliveries occurred, with 3 infants stillborn (7·5 per cent). Only 23 cases of postpartum haemorrhage were encountered, an incidence of 1·56 per cent; in one case the cause was an episiotomy with vulval varices. Thirty cases of manual removal of the placenta occurred. Caesarean section was carried out on 38 patients (incidence 2·6 per cent), 14 by the Classical operation. The incidence of forceps delivery was 6·8 per cent.

No destructive operations were performed on the foetus. Puerperal pyrexia of the genital tract was found in but 4 cases, 3 of them in patients having had a Caesarean section. The stillbirth rate was 2·92 per cent and the neonatal death rate 1·64 per cent.

No cases of special interest are recorded.

THE ANNUAL REPORT OF THE MATERNITY UNIT, ST. FINBARR'S HOSPITALS, SOUTH CORK BOARD OF PUBLIC ASSISTANCE, FROM 1ST SEPTEMBER, 1956 TO 31ST AUGUST, 1957

THIS lively report consists of summaries and commentaries of the various types of case admitted, without the use of detailed tables. That the maternity unit has its difficulties is admitted in the introduction, which states: "Once again I regret to report that nothing has been done about equipping the department with an

operating theatre. It is, at times, a most unsatisfactory and dangerous procedure to transfer patients by ambulance for Caesarean section.

"It is also to be regretted that we still suffer from the incomprehensible system of rotating staff nurses between all departments in the hospitals. This means that no section, such as the labour ward or nurseries, ever has a permanent staff. It is quite obvious that the best results cannot be obtained with the present system. In fact, it is impossible to maintain a routine."

The department delivered 1,066 patients during the year and 155 patients were delivered in their own homes. The stillbirth rate was 4·6 per cent and the neonatal death rate 2·2 per cent. A serious epidemic of poliomyelitis came under the care of the department; all the babies survived but 2 mothers died. One of these was admitted at term, comatose and cyanosed; a lower segment Caesarean section was performed and also a tracheotomy but she died on the 5th day. The other case was admitted in labour with respiratory and leg paralyses; a low forceps delivery and manual removal of the placenta was carried out. She died on the 7th day from involvement of the bulbar centres. A further 2 patients died, one from a massive pulmonary embolus a few hours after the evacuation of an incomplete abortion and the other following a post-partum haemorrhage and manual removal of the placenta.

Three cases of special interest are described; firstly, a placenta adherent to the old scar of a lower segment Caesarean section performed for placenta praevia; secondly, a lower segment Caesarean section scar that ruptured spontaneously as the utero-vesical peritoneum was being incised during a repeat lower segment section; thirdly, a case of fenestrated foetal membranes that leaked liquor from the 24–37th weeks of pregnancy when she was delivered of a live baby weighing 5 pounds.

The Maternity Unit is to be congratulated on publishing this report so quickly.

CLINICAL REPORTS OF THE MATERNITY DEPARTMENT OF GUY'S HOSPITAL, LONDON, FOR THE YEARS 1954 AND 1955

THESE reports are based on the tables recommended by the Royal College of Obstetricians and Gynaecologists for the classification of the work of maternity hospitals, but the presentation is unusual for, instead of division of cases as booked or unbooked, patients are grouped as Class A or Class B. The preface explains that Class A comprises all patients living in the Guy's Hospital Maternity District, whether delivered in their own homes or in the Hospital, and thus represents the unselected midwifery practice of a very compact district. Class B comprises patients from outside the hospital district, mostly referred because of abnormality in pregnancy or anticipated difficulty.

The 1954 report presents a summary of yearly results since the introduction of annual reports in 1928, and this summary shows that the Class A patients have almost halved in numbers, while the Class B patients have more than doubled. An interesting reflection of the change in obstetrics in the last quarter of a century is provided by comparison of the results in these two classes, for in the last four years recorded both the maternal and foetal wastage by stillbirth and neonatal death have declined most markedly in Class B; in fact, the selected abnormal patients receiving hospital management have now a more favourable outcome than the unselected district midwifery of Class A.

Although so much good work is recorded in these two years, there are also reminders of the ever-present maternal hazards of pregnancy (two maternal deaths, 0·8 per thousand patients delivered). The first of these was unavoidable; the patient, a primigravida suffering from rheumatic heart disease and third degree placenta praevia with recurrent haemorrhages, was delivered by Caesarean section and was apparently recovering safely when suddenly overcome by acute respiratory distress, presumably due to pulmonary embolism. The second patient, a healthy primigravida, had a somewhat prolonged labour, terminated by rotation and forceps delivery under general anaesthesia, without special obstetric difficulty. During induction of anaesthesia the patient, who had drunk glucose fruit drinks during labour, vomited and became "transiently cyanosed". Thereafter, in spite of most thorough efforts to clear the air passages and support the patient, pulmonary oedema developed and death ensued in ten hours. This case is a reminder that anaesthetic risk has in recent years, as a cause of maternal death, become relatively prominent in comparison with the decline of most obstetric risks.

In Table 32, Stillbirths, the information in the column headed "Remarks, and (probable) Cause of Death" is rather disappointing. Probably this is due to too much being asked of this column. The term "placental insufficiency" is prominent, and may be related to placental infarction, accidental haemorrhage, small placenta, prematurity, pre-eclampsia, postmaturity, but not in all such cases. Last in the list is the spontaneous delivery of a stillborn foetus with the comment "Pitocin Drip. Induction. Macerated" which leaves the cause of death very much in doubt.

Despite this minor criticism, there is much to admire in the presentation of these reports and particularly in the results of the treatment of Haemolytic Disease due to Rhesus Antigen, where there has been no foetal loss in two successive years.

DUNCAN MURDOCH.

BOOK REVIEWS

"Artificial Insemination in the Human." By A. SCHELLEN, M.D. Pp. xii+420, with 10 figures and 35 tables. Elsevier Publishing Company, Texas, 1957. Price 72*s*.

IF anyone wants all the facts, and a few fancies, about the history, technique, and the religious, social and legal aspects of human artificial insemination, either from husband or donor, he can find them in this book. To give some idea of the author's industry it may be stated that about 360 references appear in the text, and there is a supplementary bibliography with over 300 entries. Much detail of the technique of both A.I.H. and A.I.D. is given. The chapter on the legal aspect of artificial insemination is probably the most useful in the book, and includes references to British, American, French, German, Swiss, Scandinavian and Dutch case law. The views of the authorities of the protestant and catholic churches, and of the Jewish and Mohammedan religions are set out.

In the face of such erudition it is perhaps unfair to say that this is a most tedious book to read. The author is so anxious to omit nothing that the text seems to consist entirely of quotations of the opinions of various authorities, without any attempt at criticism or selection. On the other hand, this method of writing has the advantage that the facts are presented without any emotional bias, and it is only in an epilogue that Dr. Schellen gives his own views. Few would disagree with his opinion: "A.I.D. may in many cases produce the desired result, a child. But even if this result is considered to be an advantage and an enrichment, the means by which it is achieved are encumbered with many immoral, asocial and unnatural elements . . . Seen quite objectively, the advantages of A.I.D. do not outweigh its disadvantages."

"A Baby is Born." Pp. 62, with 32 plates. Designed and published by the Maternity Center Association, New York, 1957. Price $6.

THIS book is presumably designed for lay women who are contemplating or enjoying pregnancy. It consists of a series of extremely detailed anatomical illustrations of the pelvic organs, of the changes in the uterus and its contents during pregnancy, and of the stages of normal and breech delivery. The captions are in English, French and Spanish.

It is a little difficult to understand the purpose of this lavish series of plates. The tone is so clinical that they would be quite suitable for illustrating a lecture to midwives, but it seems doubtful whether they would help an ordinary patient. However, if any woman likes to think of herself in terms of sagittal sections these excellent and accurate plates can certainly be recommended to her.

"Obstetric Practice." By H. BRUCE WILLIAMS, Ch.M., F.R.A.C.S., F.R.C.O.G., Honorary Obstetrician, King George V Hospital, Sydney, Australia. Pp. 168. Angus & Robertson, London and Sydney, 1958. Price 21*s*.

IN this small volume, which might have been better entitled "An Obstetrician's Notebook", the author discusses the diagnosis and treatment of complications of pregnancy and labour. The text is partly in tabulated form and partly more discursive. The proof-reading has not been irreproachable. Cases from the author's long experience are cited to illustrate his views and this adds to the interest of the book. However, even allowing for differences due to the fact that "Australia is a large country with a small number of people and our base hospitals are very far distant", the course of action recommended in many instances deviates from generally accepted practice in Britain, and on this account the book is not likely to command a large public in this country.

"Having a Baby." By J. F. ROBINSON, M.B., Ch.B. Second edition. Pp. 100, with 23 figures. E. & S. Livingstone, Edinburgh, 1958. Price 6*s*. 6*d*.

IF one had to choose a single adjective to apply to this excellent little book, it would surely be "sensible". For it is a sensible book, sensibly written for sensible readers. It succeeds in its design to help young couples along the best road to parenthood; it is written in clear and practical style; and it is published at a very reasonable price.

There are short chapters on contraception and sterility, but the main content comprises advice and explanations on antenatal care, labour, puerperium and care of the newborn. It would have been helpful for the lay reader for whom the book is intended to have had included more details about current maternity grants in Britain as well as about the available services from home-helps to health visitors. Criticism can be directed to a few points only, notably the putting of the order of the possible places of delivery as (1) nursing home, (2) maternity hospital, (3) your own home. But the outstanding impression left after reading this book is that its greatest value lies in answering not only the questions women do ask, but also the questions they would like but are usually too diffident to ask.

"Before and After Childbirth, Exercises and Relaxation." By JANE MADDERS, M.C.S.P., Dip.Phys.Ed. Second edition. Pp. 31, with 35 photographs. E. & S. Livingstone, Edinburgh, 1958. Price 3*s*.

THIS beautifully produced little booklet is intended

primarily for women who cannot attend "relaxation classes". They may have difficulty in understanding some of the words (e.g., perineum), but on the whole the purpose is admirably served.

"Alexander Gordon, M.D., of Aberdeen, 1752–1799." By IAN A. PORTER, M.B., Ch.B. Pp. xii+92, with 7 illustrations. Oliver & Boyd, Edinburgh, 1958. Price 12*s*. 6*d*.

ALEXANDER GORDON's main contribution to obstetric knowledge was his "Treatice on the Epidemic Puerperal Fever of Aberdeen" published in 1795. In it he demonstrated the contagious nature of puerperal fever and advised disinfection of the hands and clothes of doctors and midwives. This was half a century before the universally recognized contributions of Oliver Wendell Holmes and Ignaz Semmelweis on the same subject.

Much of Gordon's life remains a mystery, but the author is to be congratulated on an interesting narrative which may yet place Gordon in his rightful place amongst the pioneers.

"The Year Book of Obstetrics and Gynecology, 1957." Edited by J. P. GREENHILL, B.S., M.D., F.A.C.S., F.I.C.S. Pp. 597, with 33 illustrations. The Year Book Publishers, Chicago, 1958. Price 57*s*.

THIS well-known and much appreciated annual précis of relevant world literature covers the period July, 1956 to July, 1957. All who teach, practise, or seriously study the subjects must, once more, be greatly indebted to Dr. Greenhill for his impartial summaries. Suffice it to add that this volume maintains a tradition of sterling service which extends back more than half a century.

"Psychoprophylactic Preparation for Painless Childbirth." By ISIDORE BONSTEIN, M.D. Pp. 143, with 16 illustrations. Wm. Heinemann Ltd., London, 1958. Price 12*s*. 6*d*.

THIS method, which is claimed to be an advance on "Natural Childbirth", is based on Pavlov's concept of conditioned reflexes. The book is essentially a presentation of the work of Dr. Lamaze of Paris and the collateral American series is uninspiring. Indeed it would not be unjust to say that a simple principle is completely immersed in a complex scheme of lectures, demonstrations and instructions. The mystique thus induced may be more important than the alleged scientific premise of the method. Without doubt the most impressive part of the book is the title.

"Abnormal Labour." By L. A. CALKINS, M.D. Pp. vii+70, with 6 figures. American Lectures Series. Chas. C. Thomas, Illinois, U.S.A., 1958. Price 21*s*.

THIS is a companion volume to that entitled "Normal Labour" by the same author. Brevity in this instance serves to cast into sharp relief the extent and limitations of present-day knowledge of the subject under review. While the mechanical aspects of parturition are lucidly enunciated, a lack of fundamental information of functional derangements is equally obvious and explains the vagueness of certain sections. Current British practice in the management of prolonged labour would appear to be more advanced, especially in the recognition and correction of metabolic disturbances. This, however, may be more apparent than real, due to a different standard of practice. The author's views on "Bregma presentation" are most convincing and worthy of close attention.

With minor exceptions, therefore, this slim volume contains all that the student requires on the subject and it deserves a place in the reference section of every medical library.

"Modern Trends in Endocrinology." Edited by H. GARDINER-HILL, M.D., F.R.C.P. Pp. ix+311. Butterworth & Co., London, 1958. Price 65*s*.

IN this book an attempt is made to survey some of the advances in the vast field of experimental and clinical endocrinology that have taken place in the last ten years. No claim is made that the whole field is covered, and the subjects chosen are perhaps chiefly of interest to the physician, but obstetrics and gynaecology have not been left out.

J. S. Tindal and Mary McNaught have contributed an excellent chapter on the development of the breast and milk secretion, which clearly sets out modern views on the physiology of suckling. Peter Bishop has written about the endocrine treatment of gynaecological disorders. Few would disagree with his statement that "For some years now there has been no major advance" in this field "and it seems unlikely that there will be until the mechanism of ovulation and its control in the human being is better understood, and until such knowledge can be translated into practical therapeutics". In the sense of this comment the chapter is disappointing to the gynaecologist who is seeking a simple guide to treatment, but it contains much new and useful information, not otherwise easily accessible, especially about synthetic oestrogens, progestogenic compounds and androgens. The late Kenneth Bowes contributes an erudite chapter on endocrine factors in female infertility, including a good description of the Stein-Leventhal syndrome. However, apart from Shippel's theory, no explanation of this curious clinical condition and its relief by surgery is offered.

As is so often the case in endocrinological literature, both in this chapter and in that by Dr. Bishop, the writers give numerous summaries of reports of clinical trials of various hormones but give the reader no real lead as to the best choice, or indeed of the true value of the treatments described. From practical experience many of us would feel little enthusiasm for many of the methods of hormone treatment for functional uterine bleeding, and would agree with the implications of the remark that "spontaneous remission of metropathia haemorrhagica, in the absence of treatment, is a common experience", and it is also sadly true that the hormone treatment of

amenorrhoea and anovulation is still disappointing. As regards the endocrine treatment of endometriosis this seems to the reviewer to be of little purpose except as a temporary expedient; as soon as treatment is stopped the original problem has still to be faced.

The gynaecologist today has a hard struggle to keep up with progress in his own field, and it is almost impossible for him to follow progress in other departments of endocrinology without the help of some such book as this. Scattered through it are many passing references to obstetrical and gynaecological problems, although it is noticeable how little mention is made of the hormone changes of normal pregnancy, or of the possible hormone factors in pre-eclampsia.

A chapter of great interest is that by G. C. Kennedy and R. A. McCance on endocrine aspects of over- and undernutrition. It has a disappointing lack of conclusions, but this is not because of any fault of the writers, but because of the present lack of fundamental knowledge about the subject. There is much information of potential value to the obstetrician in the chapters on fluid balance and antidiuretic hormone, and on adrenal cortical hormones by such authorities as D. A. K. Black, F. T. G. Prunty, J. E. Caughey and C. L. Cope. In the chapter on noradrenaline by H. J. C. Swan the problem of essential hypertension is approached, and the interesting remark is made that the foetal blood pressure is regulated by hormones rather than by its nervous system. The final chapter is a very fair summary of the stress concept, which now seems to appeal to many doctors, but for whose rather wide and often superficial generalizations the reviewer must admit to little appreciation, although there is much in it to stimulate thought and research.

This is a most useful book, which is likely to re-appear in successive editions to which we may look forward.

Stanley Clayton

REVIEW OF CURRENT LITERATURE

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233. **The Proceedings of the Academic Meeting of German-speaking Professors and Consultants in Obstetrics and Gynaecology held in Basle from 15th–17th October, 1957.** (Vorträge der Akademischen Tagung deutschsprechender Professoren und Privatdozenten für Geburtshilfe und Gynäkologie.)

Geburtsh. u. Frauenheilk., **18**, 295–699. Apr. 1958.

The whole of the April issue of this journal is devoted to reports of the proceedings of the conference held in Basle in October, 1957. There were 181 delegates from 9 European countries (including Germany, Holland, Switzerland and the Scandinavian countries). Eighty papers were presented and these have been published together with the ensuing discussions. Each paper has a short summary in English.

Tosetti studied, by using foetal phonocardiograms, the action on the foetus of drugs administered to the mother. He found that oxytocic drugs had no effect, that analeptic drugs led to an increase in the foetal heart rate and that morphia and pethidine produced a bradycardia, which could however be corrected if the mother breathed oxygen for 1 hour.

Stamm and Riotton have demonstrated the presence of a PAS-(periodic acid Schiff-)positive substance in the cells of the chorionic membrane, which they believe is attributable to the presence of gonadotrophins. They found that the PAS-positive substance disappeared from the chorion at term and in patients who had laboured prematurely or who had had a late abortion. In 2 cases of postmaturity the PAS reaction in the chorionic membrane remained strongly positive.

Borth and Stamm estimated the pregnanediol (100 cases) and oestriol (43 cases) content of the urine passed in the 24 hours preceding successful and unsuccessful induction of labour and before the onset of spontaneous labour. In none of these 3 groups could any difference be found in the total quantities of pregnanediol or oestriol excreted or in their ratios to each other. Napp was also unable to find any correlation between the excretion of these substances and the onset of labour.

Ten Berge made serial estimations of urinary oestriol in cases of toxaemia. The level fell with increasing severity of the toxaemia and dropped abruptly if the foetus died *in utero*. Ten Berge thinks that oestriol estimations can be used as an index of placental function.

Döring estimated the serum bilirubin in blood obtained from the placenta immediately after the birth of the baby. The average values were 3·1 mg. per cent in umbilical arterial blood and 2·86 mg. per cent in umbilical venous blood. This difference is statistically significant within the limits of experimental error and proves in the author's view that bilirubin crosses the placental barrier.

Kalkschmid presented a series of 309 cases in which oestrogens were used to induce labour for post-

maturity. All patients who were 1 week overdue were given 5 daily injections of 50,000 international units of an oestrogen preparation. The course was repeated if labour had not begun 1 week after the fifth injection. Neither surgical induction was performed nor castor oil or pitocin given to any of these patients. Labour began in 64·1 per cent of cases either during or within 2 days of the conclusion of the first course of injections. Labour had begun by the end of the second course of oestrogens in 78 per cent of the patients. The uncorrected perinatal mortality for the series was 2 per cent. The Caesarean section rate was 3·6 per cent compared with 2·3 per cent for all hospital patients.

Leinzinger demonstrated radiologically the various causes of retained placenta by injecting 70 per cent Diodone solution into the umbilical vein. If the placenta was retained *in utero* for any length of time after the injection the contrast medium passed through the placenta and excretion pyelograms of the mother were obtained.

Thomas described a method of exchange transfusion of the newborn using a 2-way catheter in the umbilical vein through which a continuous flow of donor blood was maintained, whilst the baby's blood was withdrawn through the other limb of the catheter. He left the catheter *in situ* at the conclusion of the transfusion so that repeat exchanges could be made if necessary.

Winter analyzed the cases of carcinoma *in situ* occurring in different clinics in Germany. He draws attention to the fact that exact diagnosis is difficult, since often when carcinoma *in situ* has been diagnosed from a small biopsy, evidence of invasion is in fact found later if the whole cervix is removed and becomes available for histological study. He therefore suggests that the international classification should be amended thus: Carcinoma O partialis—cases in which the diagnosis is made from smears or scrapings or from small excision biopsies; and Carcinoma O totalis—cases in which the diagnosis has been made from a complete cone biopsy or the whole cervix.

Breitner put forward a scheme for classifying all carcinomata of the female genital tract into 1 of 4 stages. It is based on the international classification for carcinoma of the cervix. The following stages were suggested: (I) the tumour is confined to the tissues of the organ of origin; (II) there is spread to the immediately adjacent tissues; (III) there is spread within the pelvis excluding the bladder and rectum; and (IV) the growth has exceeded the confines of the pelvis or involved the bladder or rectum.

Berger, Neiditsch and Mumprecht have studied squamous-celled carcinomata of the cervix with the electron-microscope. They found no differences between the cells or nuclei from cases of carcinoma *in situ* from those of invasive carcinoma.

Ludwig and Klinger described a new method (full details are given) for demonstrating the sex chromatin in mucosal smears and other tissues. They were able to show that the sex chromatin consists of 2 parts, which supports Barr's theory that the sex chromatin is derived from heterochromatic parts of the 2 X-chromosomes.

Stolte presented 2 cases of chorionepithelioma with widespread metastases both of whom failed to respond to testosterone propionate.

Hauser *et al.* have studied 19 cases in which the prolonged administration of chlorpromazine in daily doses of 200–500 mg. led to hypomenorrhoea or amenorrhoea. They found that this was characterized by a deficiency of oestrogens.

In addition to the papers presented, round-table conferences were held and are reported in detail. The subjects discussed were toxaemia of pregnancy, the placenta, the psychoprophylaxis of labour, haemolytic disease of the newborn, thrombosis, embolus and coagulation defects, new methods for the early diagnosis of cancer, radiotherapy, sterility, atypical endometrial hyperplasia, progestational steroids and the training programme for obstetricians and gynaecologists. The discussions indicate that gynaecologists in Western Europe are faced with the same problems and are dealing with them in a similar fashion to their colleagues in this country. *Peter J. Huntingford*

PREGNANCY

234. Experimental Studies on the Role of Histamine in Implantation of the Fertilized Ovum.

By M. C. Shelesnyak. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 521–537. 1957. 11 figs. 1 ref. [In English.]

The role of histamine in the process of ovum implantation in the mammal was studied in experiments designed to determine the non-hormonal factors involved in the provocation of decidual formation. Investigations revealed that histamine antagonists prevented the transformation of diploid cells into the giant decidual cells. Moreover, intra-uterine antihistamines prevented implantation and curtailed gestation, while histamine itself did not interfere. Additional proof that histamine is involved in decidual formation was obtained in recent experiments, in which the decidual reaction was produced, without surgical or physical contact with endometrium. Subcutaneous or intravenous injection of histamine, or of histamine releasers, caused the progravid endometrium of the rat to produce deciduomata. Corroborative evidence of the role of histamine in decidua formation was that at the time of nidation the uterus becomes almost depleted of mast cells (which are the sources of histamine in the body); and that a pre-implantation infiltration of the uterus with leucocytes and eosinophil cells also disappears at nidation time. *From the Author's Summary*

235. Aetiology, Incidence and Heredity of Pre-eclamptic Toxaemia of Pregnancy.

By R. Platt, A. E. Stewart and E. W. Emery. *Lancet*, **1**, 552–556. Mar. 15, 1958. 5 tables. 5 refs.

The hypothesis that antigenic incompatibility between the mother and the foetus is the cause of pregnancy toxaemia is presented. The authors investigated the incidence of toxaemia in the relatives of toxaemic women to see if there was any evidence in favour of such a hypothesis. The result of this investigation suggests that

if incompatibility exists it is not due to a single antigenic factor, but that the possibility of several antigenic factors could not be ruled out.

H. H. Fouracre Barns

236. **Studies of Water and Electrolyte Distribution in Normal and Abnormal Pregnancy.** (Untersuchungen über die Wasser- und Elektrolytverteilung in der normalen und pathologischen Schwangerschaft.)

By V. Friedberg. *Zbl. Gynäk.*, **80**, 159–171. Jan. 25, 1958. 6 figs. 2 tables. 87 refs.

The author investigated the distribution of water and sodium in non-pregnant women, in normal pregnancy and in cases of toxaemia. Intracellular water was estimated with Antipyrin, the extracellular volume with Rhodanid (thiocyanate preparation) and the plasma volume with Evans blue. The foetal water was subtracted from the values obtained according to the calculations of McCance.

The total body water was found to increase in normal pregnancy and more so in cases of toxaemia, whereas there was no significant change in intracellular water content. The extracellular fluid increased on the average by 4·4 litres. The distribution of this increase differs in normal and toxaemic pregnancies. In the former a rise in intravascular fluid (hydraemia) occurs parallel with the rise in interstitial fluid, whereas in toxaemia the plasma volume is reduced, which may lead to a distinct polycythaemic hypovolaemia. These observations were also confirmed after correction for the lean body mass. The water retention in toxaemia occurs therefore in the interstitial compartment.

The serum sodium level, estimated by flame-photometry, decreases only slightly in normal and toxaemic pregnancy, but more markedly in some cases of eclampsia with associated oliguria. The sodium level in the interstitial compartment in normal pregnancy remains slightly below the serum sodium level, whereas it often rises somewhat above that level in toxaemia. Studies of pieces of excised rectus muscle obtained at Caesarean section from a few patients suffering from toxaemia showed no change in intracellular sodium.

The author concludes that retention of water and sodium in normal pregnancy, and more so in toxaemic pregnancy, affects the interstitial compartment.

Bruce Eton

237. **Steroid Content of Urine in Pregnancy Toxaemias.** (Der Steroidgehalt des Urin bei Toxinämien in der Schwangerschaft.)

By M. Pavlatos, D. Maroudis, B. Terzis and A. Evangelopoulos. *Zbl. Gynäk.*, **80**, 391–397. Mar. 8, 1958. 2 tables. 20 refs.

The authors examined the urine of 17 patients suffering from toxaemia of pregnancy for determination of the 24 hours' excretion of phenolic compounds, "folliculin", pregnanediol and "glucuronides". They found that excretion of phenolic compounds may remain within normal limits, whereas excretion of pregnanediol and glucuronic acid compounds is reduced. In 12 cases phenolic compounds, "folliculin" neutral "17-steroids" and pregnanediol were considerably reduced. The decrease of urinary steroids of one or both groups appears to bear no relationship to the severity of the disease. Intra-uterine death is associated with a fall in both steroid groups.

As the urine of these patients contained only small amounts of creatinine, the authors suspect that apart from a placental cause of the reduced output, there is the possibility of it being due to renal insufficiency.

The authors are doubtful whether there is a relationship between the decreased production of sex hormones and toxaemia because they found that combined administration of these hormones failed to have the slightest therapeutic effect.

Bruce Eton

238. **Indications and Limitations of Hypotensive Drugs in the Treatment of Hypertension of Pregnancy.**

By M. G. H. Mayat. *S. Afr. med. J.*, **32**, 344–346. Mar. 29, 1958. 9 refs.

The author discusses the physiopathology of hypertension and the deleterious results of continued vasoconstriction. Although it has been contended that by reducing the blood pressure one may reduce the blood supply to vital organs, and that one is merely treating a symptom and not the disease, nevertheless the chief cause of maternal death is an acute cardiovascular accident which in turn is the end result of uncontrolled hypertension. The ideal drug should also improve the circulation of the brain, kidneys and the placenta. It has been shown that heavy sedation (particularly intravenous barbiturates) depresses oxygen metabolism of the brain almost to the same degree as eclampsia. The author feels that the correct indications for the use of the hypotensive drugs is (*a*) to allow time for "ripening" of the cervix by means of the pitocin drip, (*b*) in cases of pre-eclampsia occurring before the 35th week, and (*c*) in cases of essential hypertension which do not respond to rest and sedation before the 35th week.

L. J. Abramowitz

239. **Evaluation of Chlorothiazide (Diuril) in the Toxemias of Pregnancy.**

By F. A. Finnerty, Jr., J. H. Buchholz and J. Tuckman. *J. Amer. med. Ass.*, **166**, 141–144. Jan. 11, 1958. 14 refs.

Although the exact metabolic defect in toxaemia of pregnancy is unknown it seems that the factors responsible for excessive sodium retention must be implicated in some way, and rational therapy should therefore include a sodium diuretic. One hundred and forty-four patients with various forms of toxaemia were divided into 3 groups. Chlorothiazide was given alone to 85 patients, alternately with acetazolamide in 43, and simultaneously with acetazolamide in 16. The average effective dose of chlorothiazide was 1,000 mg. per day by mouth. No toxic effects were noted except for slight nausea in 7 patients. The average duration of therapy varied between three and nine weeks and the average weight loss was 3 to 4 pounds. In many cases a fall in arterial pressure was also noted.

As a result of this study the authors conclude that (1) chlorothiazide is a potent orally active non-toxic diuretic, ideal for prevention and treatment of toxaemia; (2) it enhances fluid and electrolyte excretion as efficiently as acetazolamide and reduces arterial pressure more effectively, especially when given with other hypotensive drugs; and (3) the effect of chlorothiazide and acetazolamide together is greater than that of either drug given separately. *D. W. James*

240. **Successful Pregnancy under Treatment for Malignant Hypertension.**

By P. KINCAID-SMITH, K. SOMERS and J. C. M. BROWNE. *Lancet*, **1**, 508–510. Mar. 8, 1958. 9 refs.

The authors describe the successful case of a patient with a 14-year history of severe hypertension who was delivered of a surviving premature infant after two previous episodes of malignant hypertension, one 4 and the other 14 years previously. The management consisted in administration of hypotensive drugs and the maintenance of the erect posture rather than traditional rest in bed. Premature delivery followed accidental haemorrhage when the pregnancy had lasted just over 29 weeks.
H. H. Fouracre Barns

241. **Buclizine Hydrochloride for Nausea and Vomiting of Pregnancy.**

By F. J. CONKLIN and R. E. L. NESBITT. *Obstet. Gynec.*, **11**, 214–219. Feb. 1958. 1 fig. 7 tables. 5 refs.

Buclizine hydrochloride is a new compound with antihistaminic properties. In 1956–57, 58 patients complaining of nausea and vomiting were studied at Johns Hopkins Hospital, Baltimore. Buclizine, in 50 mg. and 25 mg. doses, was found to be effective treatment and superior to other drugs tried. Thus, 31 of 32 patients treated noted complete relief of symptoms or marked improvement. Buclizine produced its effect within 24 hours in the majority of cases. The only significant side effect was drowsiness. There were no other maternal or foetal complications. *J. G. Dumoulin*

242. **One Radiograph to Exclude Placenta Praevia.**

By A. A. EARN, J. L. FREER and D. R. CAIRNS. *Lancet*, **1**, 828–829. Apr. 19, 1958. 1 table. 31 refs.

The object of the investigation of 107 patients was to find a reliable simple diagnostic method, so that those patients who were conclusively found not to have a placenta praevia could be spared a long stay in hospital. The indications for radiography were ante-partum haemorrhage, malpresentation, unstable lie or high foetal head. The placenta was correctly identified in the upper uterine segment in 90 of the 107 patients on the evidence of a single lateral radiograph of the uterus. Of the 107 patients investigated by direct and indirect placentography there were 17 with placenta praevia, which was correctly diagnosed in 12 cases and suspected in 2. The authors conclude that it was safe to allow the patients to go home from hospital when placenta praevia had been excluded by a single lateral radiograph of the uterus showing the placenta in the upper uterine segment.
H. H. Fouracre Barns

243. **Therapeutic Abortion.**

By O. SCHERMAN. *Obstet. Gynec.*, **11**, 323–335. Mar. 1958. 7 figs. 43 refs.

During the period 1949–55 there were 31,581 deliveries at the main hospital in Portland, Oregon, and 139 therapeutic abortions. The yearly incidence of therapeutic abortion has decreased, probably owing to better understanding of obstetrical complications and a greater realization that with correct therapy disease and pregnancy are compatible. Thus, far fewer terminations are being done for rheumatic heart disease and hypertensive cardiovascular disease. Severe chronic nephritis still seems to be an accepted indication, but renal tuberculosis no longer is. Similarly, pulmonary tuberculosis is a disappearing indication. These and the many other diseases associated with pregnancy are discussed by the author who shows that there is an important trend in regard to therapeutic abortion, namely, that all major organic illnesses have shown a considerable decrease in frequency as indications.

Thirty per cent of the abortions done in the author's series were for psychiatric reasons. Scherman considers it to be the least justifiable of all indications. He believes that many abortions are done for disproved and outmoded indications simply because of lack of knowledge of recent advances. Many recent writers have stressed the real need for disregarding socio-economic, "convenience", and foetal reasons from the consideration of therapeutic abortions. *J. G. Dumoulin*

244. **Sex Determination of Aborted Ova.** (Geschlechtsbestimmungen bei Abortiveiern.)

By K. W. SCHULTZE, A. BOHLE and H. VOSGERAU. *Zbl. Gynäk.*, **80**, 453–456, Mar. 22, 1958. 1 fig. 9 refs.

Histological examination of the placentae of 700 abortions revealed that 37 per cent of the ova were malformed.

Sex determination was carried out on the stroma cells rather than the trophoblastic epithelium because the latter often shows nodes of chromatin which cannot be distinguished from the sex chromatin.

In a study of 160 aborted ova and 131 placentae which were microscopically normal, the diagnosis of the sex was based on the presence of dense, basophil, planoconvex corpuscles of chromatin, with a maximal diameter of one micron, adherent to the inner aspect of the nuclear membrane.

Amongst abnormal ova, aborted spontaneously, the male sex was 8 times more frequent than the female. Amongst normal ova aborted spontaneously, the ratio of males to females was 4:1.

As would be expected, the incidence of abnormal ova was much lower in a group of 40 pregnancies terminated artificially up to the fourth month. In this group there was also a small preponderance of male ova (2·6:1).

The interesting observation was made that the predominance of male (normal and abnormal) ova was

lower during the first and second months of pregnancy than during the third.

The authors do not think that the high proportion of male ova in cases of abortion is due to a sex-linked lethal gene. *Bruce Eton*

245. Clinical Value of Serologic Examinations Related to Blood Groups in Pregnant Patients.

By K. STERN. *Amer. J. Obstet. Gynec.*, **75**, 369–375. Feb. 1958. 14 refs.

The author recommends that the first test for antibodies in the sera of an Rh negative pregnant woman whose husband is Rh positive should be done before the end of the first trimester. If antibodies are present then they are most likely a carry over from a previous pregnancy or a transfusion. If none are present the test should be repeated at approximately the sixth month and again about 4 weeks before term. The time of first appearance of antibodies is of paramount importance in connexion with their effect on the foetus. If they do not appear before the last 4 weeks of pregnancy we can be fairly certain they will not do serious harm to the foetus, but if present for at least 3 months before delivery, serious clinical disease is much more likely. Repeat tests, too, may demonstrate a rise in titre. Such a rise, if established convincingly by tests done in the same laboratory, by the same method, is almost definite proof that the foetus is Rh positive. If the antibody titre does not increase it may be due to the woman having reached the peak of her antibody production and not to the foetus being Rh negative.

Two opposing views have been expressed as to whether the height of the antibody titre is of prognostic importance. According to one view it is of no significance at all. According to the other neonatal disease can be predicted with great accuracy by the antibody titre. In the author's experience the truth lies somewhere in between. Statistically speaking, high antibody titres, provided they were present for at least 2 to 3 months of intra-uterine life, are associated with diseased infants in the majority of instances, possibly in 80 to 90 per cent. On the other hand, it is true that severe disease may occur in infants born to mothers with consistently low titres but this is rare, as is the converse. For the past 6 years the author has used what he considers is the most sensitive technique, namely, red cells treated with the proteolytic enzyme papain.

An Rh positive foetus whose red cells are incompatible in the ABO group with the mother's blood is less likely to cause maternal Rh sensitization than is one compatible in the ABO group. The reason is not known.

In all cases where Rh antibodies were absent as well as when they were present during pregnancy, it is advisable to repeat the test approximately 2 to 4 weeks after delivery. When the Rh antibodies were absent antepartum the possibility exists that antibodies will develop post-partum, for which the entry of foetal blood into the mother's circulation at delivery is presumably responsible. Detection of these is obviously important for the prognosis of future pregnancies. Similarly rises in the titre of antibodies present previously are not seldom observed post-partum, so tests at this time will furnish the most reliable base line for evaluation of antibody titres in the next pregnancy. *F. J. Browne*

246. The Outlook for Future Pregnancies in Women Immunized to Rh.

By E. L. POTTER. *Amer. J. Obstet. Gynec.*, **75**, 348–356. Feb. 1958.

In an attempt to find out the chances of procuring a surviving child from an existing pregnancy in a parous woman with an Rh incompatibility, the author studied the histories of 238 women immunized to D and 3 women immunized to C and delivered of 302 infants in the last 20 years. Excluding abortions below 400 g. weight, she found that if the patient had had an erythroblastotic infant that survived there was a 50 per cent chance that the child of the next following pregnancy would also survive; if she had had an erythroblastotic infant that died neonatally, the chance that the child of the next following pregnancy would survive was 25 per cent; and if she had had a stillborn child because of erythroblastosis the chance of a surviving child from the next pregnancy was only 10 per cent. With improvements in treatment currently taking place a somewhat larger percentage should survive in the future.

F. J. Browne

247. Mitral Valvotomy and Pregnancy.

By G. WADE, W. F. NICHOLSON and A. M. JONES. *Lancet*, **1**, 559–563. Mar. 15, 1958. 4 tables. 5 refs.

This paper is based on the study of 27 women with mitral stenosis of whom 12 were operated upon during pregnancy and 15 underwent pregnancy following valvotomy. During pregnancy the operation was performed between the 10th and 31st weeks. Five of these 12 patients were multiparae. Mitral stenosis was the sole lesion in all cases. Operation was undertaken on account of severe pulmonary congestion and severe dyspnoea on effort. Four of the patients also had attacks of nocturnal dyspnoea. No improvement occurred in one patient, another developed a right hemiplegia 6 hours after operation, active rheumatism occurred 8 days after operation in a third patient, and cerebral embolism and heart failure occurred 2 days after operation in a fourth patient who subsequently died in failure 7 weeks after operation. Nevertheless, the final assessment 6 months post-partum showed that 10 of the survivors had no cardiac symptoms. Two abortions followed operation but the other 10 pregnancies resulted in normal full-time deliveries.

There were 16 pregnancies in the 15 women who had previously had a valvotomy performed. There were no maternal deaths but four perinatal deaths of which only one was considered to be due to the cardiac condition. In spite of these good results the pregnancies were not trouble-free. Three patients experienced orthopnoea and nocturnal dyspnoea, one had severe haemoptysis, 2 frank pulmonary oedema, and another congestive heart failure. The time elapsing between operation and the completion of the pregnancy varied from 11 months to

nearly 4 years. The authors draw attention to the fact that careful re-assessment of the cardiological condition must be made if the interval is long.

They conclude that pregnancy does not appear to increase the operative risk of valvotomy; by contrast with medical treatment the operation does not increase the foetal mortality; and in suitable cases valvotomy is preferable to termination. With regard to pregnancy after valvotomy, such pregnancies are usually safe but difficulties may be encountered; a technically unsatisfactory operation is unlikely to permit of a trouble-free pregnancy; and assessment of pregnancy cannot be undertaken sooner than six months after the operation.

H. H. Fouracre Barns

248. **Severe Hemoptysis During Pregnancy Treated by Mitral Commissurotomy.**

By W. P. M. FULTON and G. SMITH. *Circulation*, **17**, 204–207. Feb. 1958. 4 figs. 5 refs.

A case is presented in which mitral commissurotomy was performed in the 5th month of pregnancy for recurrent profuse haemoptysis.

A tight mitral stenosis was relieved, the haemoptysis ceased and pregnancy continued to term without complication, and a healthy child was delivered normally.

The patient had failed to respond to conservative treatment which the authors, quoting Wood, state is the usual method of management. They consider that pregnancy and collapse of the right lung, presumably due to the aspiration of blood into the bronchial tree, contributed to the severity of the bleeding and failure to respond in their case.

The authors state that mitral commissurotomy is not often warranted during pregnancy, and where it is, pulmonary oedema has been present in most of the reported cases.

D. J. MacRae

249. **Recognition and Management of Problems Associated with Prediabetes During Pregnancy.**

By E. R. CARRINGTON, H. S. REARDON and C. R. SHUMAN. *J. Amer. med. Ass.*, **166**, 245–249. Jan. 18, 1958. 5 refs.

A latent disorder in carbohydrate metabolism may be accentuated by pregnancy and may have adverse effects on the foetus similar to those ordinarily attributed to true maternal diabetes. Because pre-diabetes is often unsuspected the foetal loss may be even higher (30 per cent) than that experienced by those patients with known and controlled diabetes.

The authors obtained glucose-tolerance tests from 790 patients whose pregnancy records suggested impairment of carbohydrate metabolism because of one or more of the following factors: (1) a family history of diabetes, (2) previous stillbirth or neonatal loss, (3) oversize infants, (4) glycosuria during pregnancy, (5) hydramnios, or (6) repeated abortion. According to the type of curve patients were classified as "suggestive" (two-hour blood glucose level 120–140 mg. per 100 ml.), "prediabetes" (140–170 mg. per 100 ml.), and "gestational diabetes" (exceeding 170 mg. per 100 ml.).

Prediabetes is treated by suitable diet and induction of labour if the two-hour blood sugar level is rising, or if hydramnios or toxaemia persist. Unfavourable signs in the infant after birth are respiratory distress, irritability, hypotonia, cyanosis, hepatomegaly, tachycardia, hypothermia, and petechiae. Skilful paediatric care is necessary in the critical neonatal period and full details of the management are given.

In this series of 790 patients there were 111 whose two-hour glucose levels exceeded 120 mg. per 100 ml. Of these 46 were detected early enough in pregnancy to permit adequate treatment and in these there were no foetal losses. Among the rest there was much neonatal morbidity, and in 39 cases unrecognized before delivery the infant mortality rate was 25·6 per cent.

D. W. James

250. **Uterine Prolapse as a Complication of Pregnancy. Case Report and a Review of the Literature.**

By M. B. MARCUS and M. L. BRANDT. *West. J. Surg. Obstet. Gynec.*, **66**, 90–93. Mar.–Apr. 1958. 11 refs. 1 fig.

After a search of the American literature 193 cases of this complication have been found, the prolapse usually being second degree (the cervix protruding from the vulva). One further case is added. The condition has little effect on fertility and conservative management with a normal delivery is advised. A pessary may help during pregnancy and repair during the post-partum period is probably the best method of treatment.

[It is probable that this condition is much more common in other parts of the world.]

D. C. A. Bevis

251. **The Surgical Management of Fibroids and Pregnancy.**

By H. A. LUSK. *West. J. Surg. Obstet. Gynec.*, **66**, 86–89. Mar.–Apr. 1958. 3 figs. 15 refs.

The author discusses his results in 22 patients with fibroids occurring in 631 deliveries; more than half were primigravidae and in the remainder the abortion rate was 25 per cent. Nineteen patients had living babies, 10 being delivered by Caesarean section.

In a series of 15,000 patients at the Hollywood Presbyterian Hospital, 112 had fibroids and 54 per cent were primigravidae. Seventy-three per cent of the babies were liveborn and there were 11 per cent of abortions. Sixty-three per cent of the patients were delivered by section.

Conservative measures are advised and the use of "sterility studies" before surgery in the non-pregnant patient is advocated.

D. C. A. Bevis

252. **Extra-Uterine Pregnancy at Term.** (Donoszona ciaza zewnatrzmaciczna.)

By J. HIGIER and A. JUREWICZ. *Ginek. polska*, **29**, 19–31. Jan.–Feb. 1958. 7 figs. 29 refs.

The author describes a case of tubo-abdominal pregnancy at term. The patient, a 26-year-old multipara,

was admitted into hospital as a case of intestinal obstruction. The correct diagnosis was made later, after the cessation of foetal movements ten days prior to the operation. On laparotomy a mature dead foetus was found, weighing 2,630 g. and 48 cm. long. The placenta was attached to the left tube, broad ligament and mesentery of the sigmoid colon, from which it was separated. It weighed 1,710 g., and was 22 cm. long, 19 cm. wide and 12 cm. thick. The post-operative complication was an infected haematoma in the pouch of Douglas which was treated by a colpotomy.

The authors describe the pathology of extra-uterine pregnancy at term, the diagnosis and treatment. Special attention is drawn to the technique of removal of the placenta. *S. H. Riterband*

LABOUR

253. **Psycho-Prophylaxis in Childbirth.** (Parto psicoprofilattico.)

Minerva ginec., Torino, **10**, Jan. 31, 1958.

This number is taken up by articles on "natural" childbirth as practised by obstetricians of many nations given at a conference in Turin. The guest president was Dr. Grantly Dick Read who gave an account of his campaign for "Childbirth without Fear", and of the reactions it had provoked.

Every paper presented, whilst advocating mental and physical instruction and training during pregnancy for labour, agreed that painless labour was quite exceptional (about 10 to 12 per cent), and that to hold out exaggerated claims could only bring disillusionment. All papers stressed that a majority of women need sedatives, relaxants, tranquillizers or analgesics at some stage, but that good co-operation was usual and of great value as a result of training in pregnancy. A suggestion worth noting was that many women gained confidence if they saw beforehand the actual scene of their confinement—a peep through the door at a quiet moment—and especially the lying-in ward when the mothers have their babies in their arms. This combined with a generally cheerful, friendly and competent attitude at the antenatal clinic is clearly the foundation to build upon.

W. C. Spackman

254. **A Comparison of Maternal and Foetal Folic Acid and Vitamin B_{12} at Parturition.**

By H. Baker, H. Ziffer, I. Pasher and H. Sobotka. *Brit. med. J.*, **1**, 978–979. Apr. 26, 1958. 19 refs.

Vitamin B_{12} is essential for proper metabolic function and plays a part of primary significance in foetal growth and tissue nucleic acid synthesis. There is also an important relationship between vitamin B_{12} and folic acid (P.G.A.) in nucleic acid synthesis.

P.G.A. has in addition an interrelated action with progesterone in pregnancy, for it prevents the inhibiting effect of P.G.A. antagonists on progesterone, which may cause foetal death.

The investigation described in this paper shows that vitamin B_{12} and P.G.A. serum levels at parturition are lower in the mother than in the infant, and it appears that the rapidly growing foetal tissues draw on the mother's supply of these vitamins with avidity. This explains the decreasing vitamin B_{12} serum levels in pregnant women noted by other authors.

R. W. Grayburn

255. **Induction of Labour: An Analysis of 1,877 Cases Done in the Maternity Hospitals under the Aegis of the University of Cape Town during the Years 1952–1956 (Inclusive).**

By B. Bloch. *S. Afr. med. J.*, **31**, 1033–1037. Oct. 12, 1957. 6 tables. 21 refs.

Methods of induction available at the present time and those employed in this series are described. Low puncture of the membranes was the method in 1,736 cases and high puncture in 138 patients. The indications for induction are discussed, pre-eclampsia and hypertension being responsible for 76·8 per cent and prolonged pregnancy for 8·5 per cent of inductions. It is felt that if induction is essential the state of the cervix should not be seriously considered. Induction was successful in 96·1 per cent of cases. The average induction delivery interval was 37 hours 33 minutes with high rupture of the membranes, and 24 hours 43 minutes with low rupture. There were 11 maternal deaths, due in the vast majority of cases to complications of pre-eclampsia or eclampsia. Nine of these deaths occurred in patients who had not sought antenatal care. The total foetal loss was 7 per cent (86 stillbirths and 47 neonatal deaths). The corrected foetal mortality was 3·2 per cent. The maternal morbidity rate was 3·9 per cent as compared with 3·7 per cent in spontaneous deliveries. The need of a high standard of asepsis and antisepsis is stressed, the tendency to rely on antibiotic cover being condemned. Prolapse of the umbilical cord occurred in 9 cases, 8 of the patients being multiparae. The post-partum haemorrhage rate was not increased. *L. J. Abramowitz*

256. **A Critical Study of 200 Cases of Pitocin Drip.** (Etude critique de 200 cas de perfusion d'extrait hypophysaire.)

By H. Vermelin, M. Braye and C. Colette. *Gynéc. Obstét.*, **56**, 402–409. Aug.–Oct. 1957. 1 table.

The pitocin drip was used in 200 cases in the Obstetrical Clinic at Nancy between 1950 and 1957; in that time there were 14,746 confinements. For the drip 5 units of pitocin were added to 500 ml. of isotonic glucose solution, and the drip was given at 20–40 drops per minute.

The indications for the use of the drip were as follows: dyskinetic cervix 162 cases, dystocia in multiparae 4 cases, cord prolapse 7 cases, placenta praevia 9 cases. Labour was also induced in 18 other cases for premature rupture of the membranes (9), very large babies (5), and for non-specified reasons in 4 cases.

The infusion was used in 160 cases of dyskinetic cervix in single pregnancies, and twice in twin pregnancy. In the single pregnancies the infusion was begun with intact membranes in 31 cases, and after rupture of the

membranes in 129 cases. In 17 cases a second infusion was required, and in 3 cases a third. The cervix was between 2 and 4 fingers dilated. Dilatation was completed in less than 3 hours in 110 cases, and in less than 6 hours in 41 cases. In these 160 cases forceps were used for 32, and manual removal of the placenta on 6 occasions.

The cases of cord prolapse during the first stage of labour were all with head presentations, and were treated by manual reposition under anaesthesia. The pitocin infusion enabled the labour to be completed spontaneously in 5 cases, and twice by application of forceps. All save one of the children were delivered alive.

In cases of hydramnios rupture of the membranes usually suffices to bring on labour, but in 4 cases pitocin infusion was used because of absence of contractions, and resulted in rapid labour in 3 cases. Two cases of premature rupture of the membranes that were not in labour after an interval of 3–4 days responded promptly to pitocin infusion.

In their earlier cases the writers stopped the infusion after delivery of the child; in later years the drip was continued to the end of the third stage. Out of 75 cases in which the infusion was kept up till the end of the third stage, exploration of the uterus for a retained placenta was only required in 3 cases.

No maternal ill effects were attributed to the pitocin, except in one case in which the patient developed an eclamptic fit at the time of full dilatation.

The "corrected" foetal mortality is stated as 11 in 155 cases (7 per cent). Only one of these foetal deaths was attributed to the pitocin, and that occurred in the case of eclampsia. The other deaths were attributed to the dyskinesis itself, and included a case of cephalotripsy for a child which died during labour, a case of version extraction, a case of Caesarean section for dyskinesis, and 5 forceps deliveries, including a case of ruptured umbilical cord, a case with the cord tightly round the neck, a case of intra-uterine infection, and two cases of intracranial haemorrhage.

[The strength of pitocin solution recommended by Theobald is much weaker than that used by the authors. The nature of the "correction" in the statement on foetal mortality is not clear.] *D. Maxwell*

257. **Synthetic Oxytocin.**

By E. H. Bishop. *Obstet. Gynec.*, **11**, 290–294. Mar. 1958. 17 refs.

Synthetic and Natural Oxytocins.

By R. H. Stewart and R. M. Slezak. *Obstet. Gynec.*, **11**, 295–302. Mar. 1958. 25 refs.

In 1953 the chemical structure of the oxytocic factor of the posterior pituitary gland was discovered. It was not long before a synthetic product was made which appeared to be chemically and biologically identical with naturally occurring oxytocin. In 1955 Sandoz laboratories named this synthetic oxytocin "Syntocinon". The trial of this product in obstetrics was reported in the above 2 papers when its effect in inducing labour was compared with that of pitocin. Each concludes that the action of the 2 medications appears to be identical. The same indications and contra-indications exist for the use of synthetic oxytocin as exist for the use of pitocin.

In the second paper it is pointed out that although Syntocinon contains no vasopressin, blood pressure effects appear to be identical with pitocin. There is, however, no possibility of a reaction from animal protein in the synthetic oxytocin. *J. G. Dumoulin*

258. **On the Possibility of Reducing the Incidence of Premature Labour.** (Lässt sich die Frühgeburtenfrequenz senken?)

By H. Wolff. *Zbl. Gynäk.*, **80**, 232–235. Feb. 8, 1958. 8 refs.

The author points out that in some patients before premature labour becomes established the cervix is taken up to a varying degree. In the case of multigravidae the cervix may admit more than one finger. This should be detected by vaginal examination until the 34th week and subsequently by rectal examination.

In the individual case the warning sign merely indicates that there is a danger of imminent labour, but not that it is about to begin.

Strict rest and progesterone therapy in these cases resulted in slight reduction in the incidence of premature labour from 5·9 to 4·2 per cent between 1954 and 1957. *Bruce Eton*

259. **Unengagement of the Fetal Head. Lumbosacral Angulation—A Pertinent Factor to be Considered.**

By J. A. Davies and E. Renning. *West. J. Surg. Obstet. Gynec.*, **66**, 61–65. Mar.–Apr. 1958. 11 refs. 7 figs.

The authors, from St. Luke's Hospital, New York, point out that during pregnancy the whole of the uterus may lie in the abdominal cavity, and as the pelvic brim is almost vertical when the patient is erect the child may lie at right angles to the pelvic cavity. A tense lower abdominal wall may prevent the child from lying horizontally and so impede entry of the foetal head into the pelvic cavity. Leaning forward and flexing the thighs may allow entry of the foetal head into the pelvis and this is aided by the contraction of smooth muscle in the round ligaments and uterosacral ligaments. On the delivery table the inlet of the pelvis is horizontal and this must be considered when delivering a breech presentation. *D. C. A. Bevis*

260. **Methods Based on the Study of Crystals and Fat Staining. Use in Diagnosing Rupture of the Membranes.**

By A. Paavola. *Ann. chir. gynaec. fenn.*, **47**, 22–28. 1958. 4 figs. 8 refs.

This is a comparison of the detection of liquor amnii by von Numers fat staining method and Neuhaus crystallization method. *D. M. Sheppard*

261. **Acute Inversion of the Uterus. A Case Report.**

By A. C. Naylor. *S. Afr. med. J.*, **32**, 196–197. Feb. 15, 1958. 7 refs.

The author describes a case of acute inversion of the uterus in a 25 year old primigravida. At previous

laparotomy the uterus had been noted to be "small, had a fundal notch and seemed to be thin walled".

A 6 pounds 6 ounces child was delivered, intramuscular ergotrate having been given on delivery of the head. The uterus contracted well after fundal massage, and the placenta was seen inside the loose dilated cervix. Two fingers were hooked round the lower placental edge and light traction made together with fundal pressure. At a second attempt there was dimpling of the fundus and inversion of the uterus occurred. Pain was severe and shock was marked. Following morphia, hydrocortisone and intravenous fluid therapy great difficulty was experienced in removing the placenta. The uterus was easily replaced with immediate improvement in the patient's condition. Inversion replacement time was about 17 minutes. The author states that the factors considered to be of major importance in this case were the small size of the uterus, the lax widely-dilated cervix and, lastly, that traction was made on the placenta. The presence of placenta accreta probably increased the risk. *L. J. Abramowitz*

262. **Puerperal Morbidity Associated with Retained Membrane and the Prophylactic Instrumental Removal of the Latter Post-Partum.**

By H. Terasvuori and E. Salovaara. *Ann. chir. gynaec. fenn.*, **47**, 29–42. 1958. 2 figs. 19 refs.

Twenty-eight thousand seven hundred and twenty-seven deliveries took place in Tampere Maternity Hospital between 1946 and 1955. Of these 957 had retained membranes (total or partial). One hundred and fifty-three of these were treated conservatively and 804 by instrumental evacuation of the uterus. The evacuation was performed on the second post-partum day, without anaesthesia, by means of ovum forceps and blunt curette. Of the cases treated conservatively only 38·6 per cent were free from infection, the remainder having symptoms varying from putrid lochia to marked puerperal endometritis with raised temperature. When evacuation was carried out 80·0 per cent were free from symptoms, almost as low a proportion as that found in a control series of normal deliveries where there was no membrane retention. *D. M. Sheppard*

ANAESTHESIA

263. **Placental Transmission of Pentobarbital Sodium.**

By J. Fealy. *Obstet. Gynec.*, **11**, 342–349. Mar. 1958. 13 refs.

Barbiturates have a hypnotic and amnesic effect on women in labour but do not reduce the level of pain. Oral administration of them gives variable results because of irregularity of absorption from the bowel. In 1946, pentobarbital sodium (Nembutal) became available for intramuscular and intravenous use. Since 1947 it has been used at the D.C. General Hospitals, Washington, as a hypnotic. Compared with thiopental sodium (Pentothal) it rarely produces laryngospasm, but it works very effectively when combined with meperidine (Demerol, Pethidine), 250 mg. intravenous Nembutal and 100 mg. intramuscular Pethidine.

In studying the babies delivered of 100 mothers given this therapy, the following facts were found:

(1) Placental transmission of pentobarbital sodium occurs almost immediately after maternal intravenous injection.

(2) Newborn blood barbiturate levels are about 74 per cent of the maternal blood levels.

(3) Blood levels of pentobarbital sodium persist at about the same equilibrium for at least 185 minutes and remain at a measurable level for at least 8 hours.

(4) Repeating the injection increases the blood level about 25 per cent in both the mother and the baby.

(5) There is no significant increase in the degree of depression of infants in using pentobarbital sodium in the above dosage: infants in the control and experimental series showed comparable degrees of alertness. *J. G. Dumoulin*

LACTATION

264. **Suppression of Lactation by a Combination of Drugs.** (Über eine komplexe Hemmung der Laktation.)

By R. Slunsky. *Zbl. Gynäk.*, **80**, 347–352. Mar. 1, 1958. 4 tables. 38 refs.

The author compares the efficiency of two methods of suppressing lactation in a series of women. One group of 50 women was treated with intramuscular oestradiol benzoate in 3 daily doses of 50,000 units each. The second group of 50 women was treated similarly with oestradiol benzoate, but these patients were also given phenergan and phenobarbital. There were less failures and a lower incidence of mammary discomfort, pain or swelling in the second group.

The author considers that oestradiol depresses the pituitary, phenergan the autonomic and phenobarbital the central nervous system. As mammary function depends on these three factors, it would explain the better results obtained with the combined method.

In the course of his investigation the author observed that the sooner after delivery the treatment was given, the more effective it was. It was most successful in women whose foetus had died *in utero*. *Bruce Eton*

OBSTETRIC OPERATIONS

265. **Cesarean Section in New York City: Incidence and Mortality During 1954–55.**

By C. L. Erhardt and E. M. Gold. *Obstet. Gynec.*, **11**, 241–260. Mar. 1958. 11 tables. 5 figs. 18 refs.

The proportion of deliveries by Caesarean section has risen in New York City from 3 per cent in 1943 to 5 per cent in 1955. The City population exceeds 8 million and the statistics reported (taken from birth and death certificates) cover 16,949 deliveries. There was considerable variation (between 4 and 6 per cent) in the section rate in different areas of the City, and among private and general ward patients. Nearly 40 per cent of the sections performed were repeat. Other indications included disproportion (30 per cent), ante-partum haemorrhage (17 per cent), and foetal distress and prolonged labour (8 per cent).

The section rate rose with advancing age of the mother from 1·9 per cent in the age group 15–19 to 16 per cent in the 45 or more group. It decreased with advancing parity, partly due, perhaps, to sterilization of some "high-risk" mothers.

The perinatal mortality rate was 38, which is 42 per cent higher than the general rate. The perinatal loss varied from 63 per cent with rupture of the uterus to 1 per cent for elective surgery in elderly primigravidae. Part of the high loss is associated with a high prematurity rate amongst the babies delivered by section.

The authors point out that great obstetric finesse is required to determine the exact stage at which delivery by section should be effected to enhance the chances of foetal survival. *J. G. Dumoulin*

266. **A Ten-Year Survey of Caesarean Sections.**
By L. G. R. VAN DONGEN. *S. Afr. med. J.*, **32**, 208–212. Feb. 22, 1958. 11 tables.

The author has investigated Caesarean section at the Queen Victoria Hospital, Johannesburg, from 1947 to 1956. In that period 786 operations were performed and the incidence rose from 1·17 per cent in 1946 to 3·47 per cent in 1956. Almost 40 per cent of the patients were primiparae. In the case of multiparae, almost 50 per cent had had a previous Caesarean section (100 had had previous classical sections and 133 previous lower-segment sections). Twenty-six of the 62 cases in the post-mature group (42 weeks or more) had abnormal presentations. The chief indications for operation in this group were disproportion in 48 per cent of the cases and foetal distress in 27·4 per cent. Of the 786 patients, over 50 per cent were not in labour. The 12 most common indications are listed. Among the 60 patients in whom foetal distress developed 17 were postmature. Information was available on the scar in 67 patients who had previous classical sections. There were 6 "rupturing scars" in this group. In 88 cases with previous lower-segment sections there were 5 "rupturing scars"—an unexpectedly high incidence. There were 3 maternal deaths (0·38 per cent), one following inhalation of vomitus, one with acute cardiac failure resulting from severe pre-eclampsia, and one patient collapsed and died of shock after the operation. There were 10 stillbirths and 37 neonatal deaths, a high percentage of the latter being premature.
L. J. Abramowitz

INFANT

267. **Male/Female Birth Ratio of Europeans in West Africa.**
By M. D. W. JEFFREYS. *S. Afr. med. J.*, **31**, 1316–1318. Dec. 28, 1957. 10 refs.

The normal male/female birth ratio for *Homo sapiens* as a genus is about 1,050 boys to 1,000 girls. Of 677 European children in Nigeria 391 were girls and 286 were boys, which gives the unusual ratio of 733 boys to 1,000 girls born. On the Jos plateau, where the altitude is 4,000 feet the ratio for European children was 1,135 boys to 1,000 girls. The normal Negro male/female birth ratio in Nigeria is 1,036 boys to 1,000 girls.

The author believes that the Y-carrying or smaller sperm is more adversely affected by certain conditions than the larger X-carrying sperm. In the European male in West Africa this may be produced by the prophylactic daily dose of 5 grains of quinine, by the general tropical environment or by some other as yet undetermined factor. *L. J. Abramowitz*

268. **Statistical Study of the Birth Rate and Infant Mortality in Belgium.** (Données statistiques sur la natalité et la mortalité du premier âge en Belgique.)
By A. TUYNS. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 495–510. 1957. 2 tables. 14 figs.

The writer analyzes the statistical data about birth rates in Belgium. An aging population, responsible for a high death rate, is shown to be related to the fall of the birth rates before World War II. After 1946 birth rates became steady at about 17 per 1,000. Infant mortality has decreased considerably; but for the first five years of life the improvement was small. The perinatal mortality is still 37 per 1,000 in 1955 and this rate could be lowered. *From the Author's Summary*

269. **Oxygenation Values in Cord Blood of Postmatures.** (Valutazioni ossimetriche sul sangue funicolare di nati da gravidanza protratta.)
By G. COLLA and C. BERTONE. *Minerva ginec., Torino*, **10**, 153–159. Feb. 28, 1958. 5 tables. 14 refs.

Oximetric studies of umbilical cord blood are the only available means of ascertaining the actual state of oxygenation of the infant at birth; and in studying the general question of postmaturity it is of special interest to know how this compares with that of the normal child born at term.

Estimations were carried out on the following three categories of infants, 60 in all, born of healthy primiparae after normal pregnancies—full-term infants, healthy babies born beyond term, and those of pathologically prolonged pregnancy (where the infants exhibited definite clinical signs of postmaturity). Some babies in each group were born naturally, others by Caesarean section. The estimations made were of total haemoglobin, oxygenated and reduced haemoglobin, saturation per cent and volume per cent of oxygen, and arterio-venous oxygen difference. From the last the coefficient of tissue utilization of oxygen which shows the relative state of oxygenation of all the foetal tissues was calculated.

Significant oxygen deficiency both in blood from the umbilical vein and in the tissues was found in all cases where "pathological" postmaturity was clinically apparent, whilst the values in normal but overdue babies did not materially differ from those of children born at calculated full term. This oxygen deficiency was shown in diminished oxygen saturation percentage, diminished oxygen volume percentage and oxyhaemoglobin, and an increase in reduced haemoglobin. The coefficient of tissue utilization of oxygen was notably reduced in "pathological" postmatures—evidence of a well-marked tissue hypoxia. The figures further show

that for postmatures elective Caesarean section gave better oxygenation figures than Caesarean section done in labour or of vaginally delivered infants, even though for the latter only peridural anaesthesia was employed.

W. C. Spackman

270. A New Device for the Resuscitation of the Newborn.

By J. E. LINDLEY. *Obstet. Gynec.*, **11**, 176–183. Feb. 1958. 4 figs. 3 refs.

The resuscitator described by the author is a boxlike structure which encloses the infant's head and body in separate, transparent, airtight compartments. The 2 compartments are divided by an adjustable sponge-rubber elastic collar which fits round the infant's neck to provide an airtight seal. The floor of the body compartment is heated from an electric light bulb. Apertures in the 2 compartments provide entrance and exit for oxygen under pressure from 2 oxygen cylinders. Pressure changes are controlled by an electronic timer, and a system of solenoid valves.

When the infant is placed in the machine a small plastic oral air-way is put in its mouth. On starting the resuscitator pulmonary ventilation with 100 per cent oxygen occurs. Flow of oxygen under pressure into the body compartment compresses the thorax and diaphragm to produce active expiration and positive pressure drainage of the respiratory tree up to 14 cm. of water. At this time the head is in a downward position and is at atmospheric pressure. The electronic timer then stops the oxygen flow in the body compartment and starts it in the head compartment. After this the oxygen in the body compartment is aspirated. Later the gases in the head compartment are drained away. The inspiratory phase lasts 2·5 seconds and the expiratory phase 1·5 seconds.

The results of an 11-month period of clinical trial of the resuscitator are encouraging. *J. G. Dumoulin*

271. Does Prolonged Pregnancy Really Increase the Perinatal Infant Mortality? (Belastet die Kindesübertragung tatsächlich die perinatale kindliche Mortalität?)

By S. KOLONJA. *Zbl. Gynäk.*, **80**, 294–311. Feb. 22, 1958. 8 tables. 88 refs.

The author reports on a study of 7,321 spontaneous single births. Amongst these were 465 children with a birthweight of 4,000 g. or more. Of these, 25·4 per cent were born between the 267th and 278th day, 25·4 per cent within two days of the expected date (the 280th), 25·8 per cent between the 283rd and 290th day, and 23·9 per cent 10 or more days after term.

The perinatal mortality of these large children was 3·4 per cent if born before term, 1·7 per cent at term, 2·5 per cent before the 10th day after the expected date and 0 per cent after the 10th day (no doubt a chance finding). Even the total perinatal mortality amongst the 7,321 spontaneous births showed no significant change before and after term. In all cases, with the exception of 15, it was possible to find an adequate explanation for the child's death which had no connexion with the factor of prolonged pregnancy.

The author feels that true postmaturity, as distinct from prolonged pregnancy, is a rare occurrence and therefore prolonged pregnancy as a rule does not carry any hazards to the foetus.

However, 15 deaths occurred amongst children born 10 or more days after the expected date. All weighed less than 4,000 g. and in at least 6 of them postmaturity cannot be ruled out.

[Large size is not the appropriate criterion for a study of the problem of the hazards of postmaturity; some postmature infants are underweight.] *Bruce Eton*

272. Abnormal Development of the Umbilical Cord and its Vessels as the Cause of Intra-Uterine Death. (Wady rozwojowe pepowiny i jej naczyn jako przyczyna obumarcia plodu.)

By J. ROBACZYNSKI. *Ginek. polska.*, **29**, 59–68. Jan.–Feb. 1958. 20 figs. 97 refs.

The author describes two cases of intra-uterine death due to abnormal development of vessels in the umbilical cord. In one case there was a local congenital stenosis of the umbilical artery with formation of a peripheral circulation in a 24-week old foetus. In the second case the cause of intra-uterine death at the 36th week of gestation was a congenital deformity of the foetus together with an abnormality of the wall of the umbilical vein.

The author points out the frequency of anatomical abnormalities in the vessels of the umbilical cord and suggests that investigations in that direction should be done more often. *S. H. Riterband*

GYNAECOLOGY

273. Pelvic Venous Pathology. I. Large Utero-Pelvic Varices. II. Paravesical Pseudotumoral Infarction. (A propos de pathologie veineuse pelvienne: 1. Enormes varices utéro-pelviennes generalisées; 2. Infarcissement pseudo-tumoral paravesical.)

By J. SIMON. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 563–574. 1957. 10 figs. 9 refs.

The author reports two clinical cases with pelvic venous pathology.

In the first case enormous widespread utero-pelvic varicosities made hysterectomy for "fibromyoma", suspected of malignant degeneration, very difficult. In fact the fibroids were found to be an extensive venous intra-myometrial lake with a muscular wall showing histological evidence of hyaline degeneration. The varicose veins exhibited some arterialization. The findings were those of authentic pelvic varicose disease.

In the other case, probably unique, pseudotumoral paravesical infarction was observed. The patient had received anticoagulant therapy one month before because of pelvic thrombophlebitis and pulmonary embolism. Differential diagnosis was very difficult and at one time, because of the rapid evolution and the cystoscopic pattern, urologists considered the possibility of a vesical sarcoma. Simple paracentesis by the vaginal route and evacuation of the old blood, resulted in cure.

From the Author's Summary

DISORDERS OF FUNCTION

274. The Surgical Diagnosis and Management of Dysfunctional Uterine Bleeding.

By E. W. MUNNELL and F. H. FLICK. *Surg. Gynec. Obstet.*, **106**, 321–332. Mar. 1958. 7 figs. 11 refs.

This is a study of 464 patients suffering from dysfunctional uterine bleeding admitted to the Sloane Hospital for Women, New York, during the years 1931 to 1945. In all cases diagnostic curettage excluded pregnancy or neoplasms as a possible cause of the abnormal bleeding.

In almost two-thirds of the cases normal proliferative or normal secretory endometrium was obtained. Cystic glandular hyperplasia was the third most common type of endometrium, being present in 13 per cent of the total. Adenomatous hyperplasia was found in 3 per cent of cases and was characterized by increased numbers of endometrial glands, glandular tufting, dense stroma and increase in the polystratified layers of endometrial cells. This was thought to be an occasional pre-cancerous lesion.

Fertility was normal in all groups prior to the onset of the dysfunctional bleeding, but thereafter was greatly lowered in the patients with endometrial hyperplasia.

Dilatation and curettage proved to be a highly effective therapeutic measure, particularly in the non-hyperplasia group where it produced immediate cure in 87 per cent of cases. In the presence of hyperplasia, however, recurrence of abnormal bleeding was common.

It is recommended that persistent or recurring dysfunctional bleeding in the non-hyperplastic group should be treated after an interval by repeat dilatation and curettage, as it carries a considerable chance of producing a cure. Because of the pre-cancerous possibilities of adenomatous hyperplasia, hysterectomy is called for as soon as the diagnosis is made. Recurrent bleeding due to cystic glandular hyperplasia should be treated by hysterectomy as it is a persistently recurring disease and fertility is very low once it has developed.

The authors believe that hysterectomy should never be chosen as the initial surgical treatment and that the use of radiation castration should be limited to those patients with persistently recurring dysfunctional bleeding who are poor surgical risks. *John P. Erskine*

275. Results of Radiotherapy in Menopausal Dysfunctional Uterine Haemorrhage Caused by Cystic Glandular Hyperplasia of the Endometrium.

By K. SOIVA and A. PAAVOLA. *Ann. chir. gynaec. fenn.*, **47**, 8–21. 1958. 15 refs.

One hundred and sixty-three patients at the provincial hospital of Turku with dysfunctional uterine bleeding due to cystic glandular hyperplasia were treated by X-ray therapy. Follow-up was carried out for an average of 8 years. Eighty-five per cent of cases were over 45. Bleeding ceased after two months in 92·9 per cent. No case required a repetition of treatment nor was hysterectomy required. Climacteric complaints occurred in 92·2 per cent but in only 23·3 per cent were these severe enough to cause the patient to seek medical attention. Sexual feelings were diminished in at least two-thirds. Five cases of malignancy were reported, one sarcoma of the body of the uterus, two cervical carcinomas, two malignant ovarian tumours. There was no case of corporeal carcinoma and the author does not consider that glandular hyperplasia is a precursor of this. *D. M. Sheppard*

276. Current Status of Relaxin.

By R. X. SANDS and M. L. STONE. *West. J. Surg. Obstet. Gynec.*, **66**, 115–119. Mar.–Apr. 1958. 10 refs.

This ovarian hormone is produced after 7–10 weeks of pregnancy and acts on connective tissue which it softens, reversing the usual aging process. It has a place in the treatment of dysmenorrhoea and may be useful in stopping premature labour. It is possible that it might soften adhesions in the tubes and so help the infertile patient, and by a similar mechanism, relax the cervix in delayed labour.

[The references are the most useful part of this article.] *D. C. A. Bevis*

277. The Endometrial Receptivity to Ovarian Hormone Modified by the Anaesthetic Infiltration of the Superior Sympathic Cervical Ganglion.

By M. CUSI. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 461–466. 1957. 1 table. 9 refs. [In English.]

In this paper the author reports the result of infiltration of the cervical sympathetic ganglion in six patients who suffered a lack of endometrial sensitivity to the corpus luteum hormone.

He has observed that the method raises the endometrial sensitivity to the ovarian hormones.

From the Author's Summary

278. A Comparison Between the Effect of Oestriol in Minimal Amounts and Total Ovarian Extracts. (Ein Vergleich zwischen der Wirkung von Östriol in kleinsten Mengen und Ovarialtotalextrakten.)

By K. A. HÜBNER and A. PUCK. *Zbl. Gynäk.*, **80**, 459–462. Mar. 22, 1958. 3 figs. 5 refs.

In a previous study the authors had found a similarity between the action of oestriol and total ovarian extract. This extract contained in 20 ml. an average of 11·1 γ of oestriol with a range of 7 to 20 γ.

Accordingly, in a series of nulliparous adult castrated female guinea-pigs some animals were injected with 20 ml. of ovarian extract, others with 10 γ of oestriol and a third group with 20 γ of oestradiol. The animals were killed after 2 days and their uteri, cervices and vaginae were studied histologically.

Oestradiol was found to have caused considerable growth of all layers of the uterus whereas oestriol and total ovarian extract had little effect. In the cervix and vagina oestradiol produced mainly proliferation of epithelium. This was less pronounced after oestriol and ovarian extract. Oestriol caused marked intra-epithelial formation of mucus.

The authors conclude that total ovarian extract and oestriol act mainly on the lower parts of the genital tract. These experiments suggest that the pharmacological and clinical effects of total ovarian extracts may be due to their content of oestriol. *Bruce Eton*

279. **Induction of Ovulation in the Human: Therapeutic and Diagnostic Importance.**

By H. S. KUPPERMAN, J. A. EPSTEIN, M. H. G. BLATT and A. STONE. *Amer. J. Obstet. Gynec.*, **78**, 301–309. Feb. 1958. 7 figs. 13 refs.

Founded on the observations that FSH stimulates production of oestrogen by the ovarian follicle, that oestrogen when it reaches a certain level inhibits FSH and releases LH which causes ovulation, that after ovulation luteotrophic hormone is produced to maintain the life and function of the corpus luteum which produces progesterone, that progesterone inhibits release of LH and so prevents supra-ovulation, the authors felt that specific hormone therapy in properly selected cases of failure of ovulation due to inadequately developed follicles producing too little oestrogen might trigger the defective ovulatory mechanism. Only patients with normal thyroid and adrenal function and who menstruated fairly regularly, or who had a proliferative endometrium as shown by withdrawal bleeding after intramuscular injection of 100 mg. of progesterone, and in whom pregnanediol was absent, were judged as having ovulatory failure due to inadequately developed follicles unable to produce the critical level of oestrogens necessary for LH release, and as being potentially responsive to a large dose of oestrogens. To these 20 mg. of conjugated oestrogens (equine) were given in a single intravenous dose not sooner than the 18th day of the menstrual cycle. An ovulatory response was ascertained by (1) a significant rise in basal body temperature (BBT) 1 to 13 days after injection and lasting at least 12 days (this alone was never accepted as proof of ovulation); (2) an increased pregnanediol excretion 7 to 10 days after injection; (3) secretory endometrium on biopsy on the first day of the ensuing period, or (4) conception. Of the 40 patients treated 31 were suffering from infertility and 9 were either single women with menstrual irregularities, or married and practising contraception with the same complaint. Nine pregnancies resulted among the 17 infertile women in whom ovulation was induced after 2 injections. In these the infertility had lasted 2 to 7 years (average 4·3 years) and in 4 of them the pregnancy occurred during the cycle subsequent to the oestrogen-induced ovulation.

It was therefore evident that the treatment could not only induce ovulation in the cycle in which it was given but was also effective in keeping the pituitary ovarian cycle self-perpetuating, at least for a limited time. In addition to the patients who became pregnant an ovulatory response was obtained in 11 others. In 16 there was no response and in 4 follow up was inadequate. It was postulated that the failure in the 16 patients was due to a mechanical inability of the ovary to respond because of the Stein-Leventhal syndrome. In 8 of these a wedge resection has been done to date, and following this all have had regular menses save 3 who became pregnant.

The authors emphasize the importance of critical selection of the patients for this therapy. All the criteria of normal thyroid and adrenal function must be satisfied and there must be evidence of an adequate proliferative phase. *F. J. Browne*

280. **Mittelschmerz or Ovulation Pain.**

By G. P. CHARLEWOOD. *S. Afr. med. J.*, **32**, 261–262. Mar. 8, 1958. 4 refs.

The author states that appendicectomy in a certain hospital was performed more than twice as often in women than in men in the 14–25 age group. It is suggested that in many cases the pain was due to mittelschmerz. In many such cases unnecessary ovarian operations are performed at laparotomy. "Bad surgery begets surgery."

The most likely cause of the pain is raised intra-ovarian tension immediately before ovulation. Important in the diagnosis is the time of onset in relation to the cycle, the fact that it has never occurred during menstruation and reproduction of the same pain by bimanual compression of the ovary.

With regard to treatment, explanation, sometimes with the help of an analgesic, is all that is necessary. In a very small minority of cases where the diagnosis is in doubt a laparotomy may be necessary. Ovarian and pre-sacral neurectomy should then be performed. The author has treated 3 cases in that manner and in a further 4 cases ovarian neurectomy only was performed, with uniformly good results. It is felt that the medical schools and textbooks are largely to blame for the lack of awareness of this condition among practitioners. It is not given the emphasis which it deserves.

L. J. Abramowitz

281. **Haemorrhagic Diathesis Due to Increased Capillary Fragility Secondary to Ovarian Deficiency.**

By R. WELLS. *Lancet*, **1**, 886–887. Apr. 26, 1958. 14 refs.

A case is described of a woman in whom a haemorrhagic diathesis developed. This commenced after oöphorectomy for an ovarian cyst and responded to oestrogen therapy. The other ovary was observed to be atrophic at the time of operation and in view of the response to oestrogens, the author concludes that the increased capillary fragility was secondary to ovarian deficiency. *H. H. Fouracre Barns*

282. **A Case of Male Pseudohermaphroditism. Biochemical Investigation.** (Un cas de pseudo-hermaphrodisme mâle. Exploration biochimique dynamique.)

By J. FERIN, R. VANEK, J. VASSILOPOULOS and A. VAN GANSEWINKEL. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 548–562. 1957. 2 tables. 7 figs. 23 refs.

In a young eunuchoid girl with primary amenorrhoea and elevated urinary gonadotrophin excretion, a virilization syndrome developed. The normal urinary pregnanetriol level and the 17-ketosteroid-chromatogram, typical of a male adult, contradicted the hypothesis of an

adrenocortical dysfunction and suggested a gonadal anomaly. Modifications of the chromatogram after administration of A.C.T.H., chorionic gonadotrophins and methylestrenolon were in accordance with the latter supposition. As the chromosomal sex was found to be male, the final diagnosis was puberty crisis in a male pseudohermaphrodite. Extirpation of the gonads was resorted to. They proved to be small abdominal testes with Leydig cell hyperplasia and important anomalies of the seminiferous tubules. The female type genital tract reacted normally to ethinyl-oestradiol therapy and bleeding was brought about by the administration of 5 mg. of methylestrenolon in five days.

From the Authors' Summary

283. **Masculinization of the Female Foetus.**

By L. WILKINS and H. W. JONES. *Obstet. Gynec.*, **11**, 355. Mar. 1958.

In a letter to the Journal, an abstract of which is given because of its possible importance, the above writers point out that oral progestin (17-ethinyl testosterone), which is marketed under the names Ethisterone, Pranone, Progesterol, Lutocylol and Duosterone, can produce masculinization of the female foetus. They have observed 17 female infants showing at birth partial masculinization of the external genitalia consisting of an enlarged phallus with or without varying degrees of fusion of the labioscrotal folds. In 12 of the cases the mother had been treated because of threatened or habitual abortion with an oral progestin, usually in large doses from early in pregnancy, and in 2 other cases intramuscular progesterone had been given.

The writers, who are submitting a paper to the *Journal of Clinical Endocrinology and Metabolism* giving details of these cases, believe that the female foetus is affected only in occasional mothers who receive these steroids.

J. G. Dumoulin

INFECTIONS OF THE REPRODUCTIVE ORGANS

284. **The Problem of the Diagnosis of Genital Tuberculosis in the Female.** (Das Problem der Diagnose der Genitaltuberkulose beim Weibe.)

By A. ALDEA, A. CRISTEA and I. FILIPESCU. *Zbl. Gynäk.*, **80**, 511–520. Mar. 29, 1958. 4 tables.

This is an evaluation of a number of diagnostic laboratory methods, based on a study of 48 confirmed cases of genital tuberculosis observed during the three-year period 1952 to 1955. The diagnosis was proved bacteriologically in 34 patients (70·8 per cent) and on histological examination of endometrium in 33 cases (68·9 per cent) suggesting that statistically the two methods have very similar diagnostic value.

In 22 patients histological and bacteriological findings were positive. In 11 cases biopsy findings were positive but bacteriological examination was negative. In 12 patients the reverse was the case. In the remaining 3 cases (6·3 per cent) both diagnostic methods failed to show evidence of tuberculosis which was subsequently proved on histological examination of the adnexa removed surgically.

Bacteriological examination was carried out on vaginal secretion, menstrual blood, cervical secretion, blood obtained during biopsy and fluid aspirated through the posterior fornix. Direct microscopy of the specimens obtained was negative in all cases. The positive bacteriological diagnosis was based on culture and animal inoculation.

The authors conclude that the two diagnostic methods do not replace each other but are complementary. The histological method should be used if bacteriological findings are repeatedly negative. *Bruce Eton*

285. **Re-Examination of Controversial Questions Relating to Genital Tuberculosis in the Female.** (Neue Untersuchungen und Gesichtspunkte in den einzelnen Streitfragen der weiblichen Genitaltuberkulose.)

By A. ARVAY and S. SURANYI. *Zbl. Gynäk.*, **80**, 521–532. Mar. 29, 1958. 6 tables. 53 refs.

Amongst 36,888 patients admitted to the gynaecological department during the 25 years between 1932 and 1956 there were 561 cases of confirmed genital tuberculosis (1·52 per cent). Of 60 patients, in whom the type of tubercle bacillus was investigated, 20 (33 per cent) were found to be infected with the bovine bacillus.

The authors believe that surface spread from the tube to the uterus is a not uncommon occurrence because in 11 out of 73 patients, in whom repeated curettage failed to provide evidence of tuberculosis, culture of intermenstrual secretion yielded positive findings, suggesting that the bacteria originated from diseased tubes. Additional evidence for this view is provided by the fact that the uterine ostium of one or both tubes was found to be patent in 82 per cent of 106 cases of proved genital tuberculosis, subjected to hysterosalpingography.

The problem of diagnosis is discussed in detail. The clinical approach should be the starting point of diagnosis (primary or prolonged secondary sterility, amenorrhoea, adnexal swellings in virgins, exudates in the true pelvis, particularly following a history of erythema nodosum, pleurisy, tuberculous peritonitis or other pulmonary or extra-pulmonary conditions). The most practical and harmless diagnostic methods are bacteriological culture and animal inoculation. Collection of intermenstrual secretion is particularly useful for this purpose.

Comparison of diagnostic methods in 73 proved cases of genital tuberculosis showed histological examination to be the most efficient, but bacteriological investigation has considerable practical value as it detects a few positive cases where histology fails to establish the diagnosis.

The authors consider that medical treatment should be continued for at least 12 months with a daily dosage of 5 mg. of INH and 0·2 g. of PAS, per kg. of body-weight. Streptomycin should be used for special indications only (fresh exudative processes, immediate danger to life, evidence of miliary dissemination, failure to respond to routine therapy and as a pre- and post-operative treatment).

Of 35 cases in which sensitivity tests were carried out, resistance to streptomycin developed in 5 and to INH in 9, i.e., 40 per cent.

The authors warn against the use of oestrogens in large doses in tuberculous subjects as they observed severe exacerbations including miliary dissemination following hormone therapy. [No details given.]

The strengthening of the general resistance of the body includes a diet rich in milk, vegetables and vitamins.

Criteria of cure are negative endometrial biopsy, and negative cultures of menstrual blood and intermenstrual secretion, repeated during several cycles. If antibiotic therapy fails to effect a cure after 12 months, surgery is justified, as it is also if the patient tolerates conservative treatment badly, if symptoms increase and if fistulae fail to close. On these grounds 27 operative interventions were carried out.

The authors point out that every woman suffering from proved genital tuberculosis should be given careful explanation regarding her infectious condition. She should not be employed in kitchens, in the handling of food, and the care of infants and young children. The possibility of such patients transmitting bovine infection to cows should be kept in mind by those responsible for the control of the disease in cattle. *Bruce Eton*

286. **Symposium on Trichomonas Vaginalis, Rheims, May, 1957.**

Gynéc. prat., **6**, 361–497. 1957.

The whole of this issue is devoted to the trichomonas vaginalis and stems from the symposium held at Rheims in May, 1957. In it are contained fourteen articles covering many aspects of trichomonal infestation in both sexes and at all ages. The social and epidemiological aspects are also well covered. Each of the articles contains points of interest, but there is, inevitably, a good deal of repetition and for this reason it seems preferable to review the issue as a whole, rather than to present abstracts of each paper.

All the authors who make reference to the point agree on the magnitude of the problem and feel that whilst the infection is not so dangerous as syphilis and gonorrhoea, by virtue of its very frequency it merits greater attention than it has hitherto received.

There is a general feeling that the infection is transmitted venereally in almost all cases but that accidental contamination can and does occur. It is seen in neonates during the period when oestrogen activity is high but then becomes extremely rare until the advent of the menarche results once more in a well oestrogenized vagina.

The clinical features of the infestation in both sexes are dealt with. It is stated that 78 per cent of the male partners of patients having trichomonas vaginitis are infected and will remain so until treated. Symptoms in the male may vary from none at all to a purulent urethral discharge which is often labelled, "penicillin resistant gonorrhoea".

Diagnosis is most easily made by the examination of a "wet slide" preparation of the vaginal secretion in the female, or in the case of the male, of the urethral secretion obtained by massage some hours after micturition. The importance of the use of stained preparations and cultures is emphasized, especially in cases, clinically suggestive, but with negative "wet films" and as a test of cure.

With regard to treatment, opinion appears nearly unanimous that the vaginal lesion is better treated locally. The results of oral therapy have been disappointing. The oral preparations, especially Trichomycine, a trichomonicidal antibiotic, are effective however in the treatment of infestations of the urinary tract.

Their value in the treatment of the male seems to be as yet unproven. Some authors report satisfactory results while others maintain that, in their cases, local therapy has given much better results.

The last article in the journal is devoted to a consideration of the possible errors introduced into the interpretation of vaginal cytological smears by the presence of trichomonas vaginitis. This may lead to an erroneous diagnosis of carcinoma *in situ* and renders smears taken for the purpose of hormonal assessments completely unreliable. *Geoffrey Dixon*

287. **Natural Lysis of Trichomonas in Vaginal Secretions.** (La lyse naturelle des trichomonas dans les sécrétions vaginales.)

By R. Bourg. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 474–480. 1957. 3 figs. 3 refs.

Trichomonads in vaginal smears show a variable but sometimes very pronounced lysis. Various morphological aspects of this phenomenon are described which may represent an immunological reaction but have not received attention from bacteriologists. The fermentative activity of the luxuriant bacterial flora may be the cause. *From the Author's Summary*

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

288. **Influence of Termination of Pregnancy, Castration and Sex Hormones on Tumour Growth.** (Beeinflussung des Geschwulstwachstums durch Schwangerschaftsunterbrechung, Kastration und Sexualhormone.)

By H. Frohberg. *Zbl. Gynäk.*, **80**, 191–201. Feb. 1, 1958. 2 figs. 7 tables. 32 refs.

After inoculating 93 pregnant rats with Yoshida-sarcoma, the appearance of a tumour of standard size was on the average delayed until the 18th day, whereas it took 10 days in 106 non-pregnant controls; the average survival time was 34 days in the pregnant animals and 25 days in the controls. In the post-partum period growth was accelerated.

Similar observations were made with Ehrlich's carcinoma in mice. Delay was also observed in animals whose pregnant uterus was removed.

Treatment of non-pregnant animals with oestradiol before injecting a tumour suspension did not influence the rate of appearance of the tumour.

The author concludes that the delaying effect of pregnancy is due to progesterone derived from corpora lutea which remain active for some time after hysterectomy. In non-pregnant mice treated with progesterone the appearance of the tumour was delayed. In 9 mice

injected with 1,000 μg. of progesterone on alternate days the Ehrlich cancer failed to grow altogether.

The influence of gonadotrophic hormones was investigated indirectly by castration which leads to a high output of pituitary gonadotrophic hormone. This procedure failed to cause any change in the rate of tumour growth.

Testosterone injected simultaneously with, or after, tumour inoculation, delayed tumour growth in a few female mice. Hormonal "castration" of females with testosterone retarded tumour growth. *Bruce Eton*

289. **Clinical Experiences with Intra-Peritoneal Radiogold Therapy.** (Klinische Erfahrungen mit der intraperitonealen Radiogoldtherapie.)

By H. Desch. *Zbl. Gynäk.*, **80**, 569–574. Apr. 5, 1958. 3 figs. 2 tables. 16 refs.

Fourteen women with incurable malignant intra-abdominal tumours and diffuse peritoneal, omental and liver metastases were treated with intra-peritoneal radioactive gold according to the technique of J. H. Müller. In 6 of these women, ovarian tumours were removed shortly before the treatment. Of 11 women suffering from ovarian carcinoma, 5 died within 6 to 15 months and 4 were free from symptoms during a follow-up period of from 5 to 22 months.

Amongst 9 patients suffering from considerable ascites there was no effect on the rate of reformation of the fluid in 3 patients; in 3 others it was distinctly reduced and in the remaining 3 completely arrested for a period of 6, 18 and 22 months respectively.

The author concludes that radioactive gold has a place in the palliative treatment of intra-peritoneal carcinomatosis.

[There may be a place for intra-peritoneal insertion of radioactive gold even after apparently complete removal of ovarian carcinoma. It may destroy viable cancer cells spilled in the course of operation.] *Bruce Eton*

290. **Studies of the Hormonal Influence of Hypophyseal Transplants in Cases of Advanced Carcinoma of the Female Genital Tract.** (Untersuchungen über den hormonalen Einfluss von beim fortgeschrittenen weiblichen Genitalkarzinom vorgenommenen Hypophysenimplantationen.)

By I. Nyiri. *Zbl. Gynäk.*, **80**, 445–452. Mar. 15, 1958. 2 figs. 34 refs.

Calf hypophyses were transplanted into women suffering from advanced genital carcinoma with the object of relieving pain. The author attempted to find out whether the beneficial effect was due to changes in the production of gonadotrophic and androgenic hormones. In 36 patients daily biological estimation of gonadotrophin output was carried out, beginning a few days before transplantation. A rise was observed in only 5 patients.

The author also wanted to see whether the transplanted hypophysis had any effect on the suprarenal gland, by determining the excretion of 17-ketosteroids. The latter were raised by more than 10 per cent in 20 of the 36 patients. The rise was attributed to A.C.T.H. released from the transplanted hypophysis. The possibility of this being due to a stress effect of the operation was ruled out as the maximum rise always occurred on the fourth day or later.

The author recommends the transplantation of the hypophysis as a method of palliative treatment for pain in these patients. *Bruce Eton*

291. **Cytological Study of Carcinoma of the Vulva After Radiotherapy.** (Etude cytologique d'un carcinome vulvaire irradié.)

By R. Bourg, R. Schoysman and M. Petit. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 511–518. 1957. 7 figs.

A patient (aged 85) received a full dose of irradiation with radium on a vulval epithelioma and the case was followed up by repeated smears until a month after the last radium application.

The smears gradually changed and four days after the treatment there was a maximal histiocytic response with nuclear degeneration. Forty days after the first application cytological cure seemed to be attained.

From the Authors' Summary

292. **Cytology and the Diagnosis of Cancer at the 1st University Gynaecological Clinic of Vienna.** (Die Zytologie im Rahmen der Krebsdiagnostik an der 1. Univ.-Frauenklinik Wien.)

By R. Klein, E. Kofler, H. Kremer and G. Rhomberg. *Geburtsh. u. Frauenheilk.*, **18**, 264–270. Mar. 1958. 3 tables. 2 figs. 25 refs.

From September, 1954 to June, 1956 the vaginal cytology of 10,688 patients was studied and in addition, colposcopy and colpomicroscopy were carried out. Papanicolaou stain was used to study smears obtained from the secretions of the posterior fornix and cervical canal and from scrapings of the portio vaginalis of the cervix in each patient.

In 414 patients (3·8 per cent) the presence of a carcinoma of the genital tract was confirmed histologically. These included 261 cases of invasive or pre-invasive carcinoma of the cervix and 42 cases of carcinoma of the corpus uteri. The cases formed approximately equal groups when they were analyzed in 3 consecutive 7-monthly periods (groups I–III). In group I the cytological diagnosis was correct in 72·6 per cent of cases. This figure rose to 79·3 per cent in group III. Expressing this improvement in accuracy of diagnosis with increasing experience in a different way, the authors found that the total of false negative and positive results fell from 27·4 per cent in group I to 20·7 per cent in group III. Of the 414 cases of carcinoma of the genital tract, cytology gave a false negative result in 24·6 per cent. In the 10,274 cases with no carcinoma a false positive diagnosis was made in 1·4 per cent. False positive results were obtained from patients with cervical erosions, chronic cervicitis, cervical or corporeal polyps, metropathia haemorrhagica, ectopic pregnancy, etc. The improvement in diagnosis was reflected by the fact that there were 116 false positives in group I and only 16 in group III.

The figures so far quoted detract from the accuracy of vaginal cytology as a diagnostic aid, since they include carcinomata of the uterine appendages. Thus, in cases of carcinoma of the cervix an accurate cytological diagnosis was made in 84·8 per cent in group I and in 93·7 per cent of cases in group III.

Twenty-eight patients were found to have a pre-invasive carcinoma of the cervix after ring biopsy or serial section of the amputated cervix. In 4 of these cytology had given a negative result. In the other 24 cases the smears examined could not be distinguished from those of an invasive carcinoma of the cervix.

The authors believe that the 3 diagnostic aids of cytology, colposcopy and colpomicroscopy are complementary to each other. They quote no figures for the accuracy of diagnosis by colposcopy or colpomicroscopy, but make the point that of 100 cases of carcinoma of the cervix examined by all 3 methods, 3 were unsuspected until cytology was performed. *Peter J. Huntingford*

293. **Rectal and Bladder Injuries Following Radium Therapy for Carcinoma of the Cervix at the Radiumhemmet.**

By M. J. Gray and H. L. Kottmeier. *Amer. J. Obstet. Gynec.*, **74**, 1294–1303. Dec. 1957. 8 tables. 18 refs.

Five hundred consecutive cases of cancer of the uterus treated in 1953 and 1954 were followed up for 1 to 3 years. Of these 1·8 per cent had bladder ulcers, or areas of necrosis or prolonged cystitis, and 3 of them developed vesicovaginal fistulas; 13·2 per cent had serious rectal injury including ulcer and stenosis, with pain, bleeding, tenesmus or diarrhoea, and there were an additional 7 cases with rectovaginal or rectovesical fistulas.

In general the extent of the injury could be correlated with the stage of the disease and the radium dosage. Above 5,000 r the rectal injuries became 18·5 per cent and there was an abrupt rise when the total dose of radium and X-rays exceeded 6,000 r. There was an abrupt rise in bladder injuries when the bladder mucosa received more than 7,000 r.

Intensity of treatment was also important. Thus if the same dose was spread over 24 to 30 hours instead of 22 hours or less the incidence of rectal injury was decreased from 22 per cent to 9 per cent. A dose of 2,400 r to the rectum in 24 hours is the maximum that should be used. *F. J. Browne*

294. **Mucosal Polyps of the Endometrium.** (Contribution à l'étude des polypes muqueux de l'endomètre.)

By P. Quevrin. *Bull. Soc. roy. belg. Gynéc. Obstét.*, **27**, 481–494. 1957. 7 figs. 11 refs.

From a study of 33 cases of endometrial polyp the following conclusions are drawn.

(1) Hysterography with organic iodine compounds is the basis of the diagnosis, but it is essential to take several pictures including a lateral or oblique view.

(2) All stages between diffuse hyperplasia, localized polypoid hyperplasia and single polyp exist, the last usually being a sequel of a previous hyperplasia.

(3) Endometrial polyps are removed with Guisez' forceps, by curettage or by a combination of both procedures.

(4) Study of the endometrium occurring in conjunction with the polyp may indicate further hormonal treatment for prevention of relapse.

From the Author's Summary

295. **Urological Complications of Stromal Endometriosis.**

By C. A. Macfarlane, C. V. Hodges, H. V. Anderson and R. C. Benson. *J. Urol.*, **79**, 436–446. Mar. 1958. 5 figs. 31 refs.

A single nulliparous woman was seen 8 years after a hysterectomy for stromal endometriosis. She was found to have a large abdominal mass above the pubes and several nodular growths in the bladder obstructing both ureters. Bilateral nephrostomy was performed and high voltage therapy given which reduced the size of the abdominal mass. There was no relief to the ureteric obstruction and an anterior exenteration was performed with transplantation of the ureters into an ileal bladder. At operation both ureters were found to be obstructed but there was no invasion of the mesocolon and no infiltration of the peritoneum. There was a large solid tumour in the right ovary.

The literature is reviewed and the first recorded case was that of Down and Lockyer in 1908. Only 102 cases have been reported. No mention is made of any bladder biopsy being performed. *J. H. Carver*

OPERATIONS

296. **Experimental Substitution of an Isolated Segment of Ileum for the Uterine Tube. A Preliminary Report.**

By M. L. Carey, L. C. Cian, H. J. Davis, B. Böving and H. W. Jones, Jr. *Obstet. Gynec.*, **11**, 156–163. Feb. 1958. 12 figs. 9 refs.

In this experiment, which was carried out on 15 rabbits, an intestinal segment was isolated from the terminal ileum. Continuity of the ileum was re-established by end-to-end ileoileostomy. A salpingo-oöphorectomy was done on the right side, and a salpingectomy on the left. The left ovary was secured to the proximal end of the tube of ileum. The other end of ileum segment was sutured end-to-end to the uterus on the left side.

Five rabbits died soon after the operation, and another 5 during the next 12 months from coincidental disease. The remaining 5 animals were sacrificed 8 to 10 months post-operatively at 10 to 20 hours post-coitum. The animals showed no pelvic adhesions; in every case the ileo-uterine anastomosis was patent; active peristalsis was present in the segment and motile sperms were found in it. There was no evidence of endometritis from ileal secretions.

The authors are trying similar experiments on monkeys.

J. G. Dumoulin

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